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CEREBROVISCERAL AND BEHAVIORAL PHYSIOLOGY AND CONDITIONED REFLEXES

General Editor: S. A. CORSON

Volume 1

COMPENSATORY ADAPTATIONS, REFLEX ACTIVITY, AND THE BRAIN

Compensatory Adaptations Reflex Activity, and the Brain

by

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FOREWORD

To those who are concerned with the development of international and intellectual exchange, it is good news to know that the Pergamon Press is producing a series of monographs on cerebrovisceral and behavioral physiology and conditioned reflexes to be edited by Professor Samuel A. Corson. These books will offer English-speaking scientists an admirable opportunity to become acquainted with significant progress among Russian and associated physiologists on a matter of increasing importance in understanding mammalian functional activity. The complex adaptive feedback mechanisms whereby the mammalian body is maintained in an internal steady state, consistent with its capacity, is a matter of ever-increasing significance, especially as we continue to probe the possibilities of human space exploration.

Actually, cerebrovisceral physiology and conditioned reflexes have been studied by English-speaking clinicians under the rather cumbersome term "psychosomatic medicine." This clinical study has not had as satisfactory a scientific foundation as the more systematic investigation of inter-relations of the central nervous system and visceral function undertaken so carefully by a great number of important Russian and associated physiologists who have followed the indications suggested by Ivan P. Pavlov (1849—1936).

Among these distinguished neurophysiologists is Ezras Asratovich Asratian, Director of the Institute of Higher Nervous Activity and Neurophysiology of the U.S.S.R. Academy of Sciences in Moscow. Professor Asratian has summarized much of his own studies in the volume *Compensatory Adaptations, Reflex Activity, and the Brain*, now so skillfully and helpfully translated and edited by Samuel A. Corson of The Ohio State University College of Medicine.

Professor Asratian's volume gives the clue to the significance of cerebrovisceral physiology in his phrase "compensatory adaptations". It is characteristic of the broad generalizing tendency of Russian and associated neurophysiologists that they should bring together concepts derived from Charles Darwin (1809–1882), Claude Bernard (1813–1878), and Walter B. Cannon (1871–1945), as well as from their own Ivan M. Sechenov (1829–1905) and Pavlov.

Professor Corson gives an admirable historical background for the philosophical orientation given to Russian mammalian biology and medicine by Sergei P. Botkin (1832–1889) and Sechenov, who were pupils of the great German physiologists, Karl Ludwig (1816–1895), Hermann von Helmholtz (1821–1894) and Emile Du Bois-Reymond (1818–1896) in Berlin. These were leaders in the materialistic approach to living processes.

Professor Corson had the opportunity to observe Professor Asratian's laboratory and his translation resulted from the inspiration he received there. It is warmly to be hoped that this initial volume in the proposed monograph series on cerebrovisceral and behavioral physiology will be followed by many others as stimulating. The Pergamon Press deserves wide support for its contributions to the promotion of effective international intellectual exchange. Professors Asratian and Corson well merit the thanks of biological scientists everywhere for their collaboration in presenting informative material of great importance for an understanding of modern physiological developments.

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CHAUNCEY D. LEAKE

EDITOR'S PREFACE

THIS book represents the first of a series of carefully selected and edited English translations and surveys of Russian contributions in the fields of conditioned reflexes and cerebrovisceral and behavioral physiology. The preparation of these surveys and translations has been made possible by a research grant to the editor from the National Institutes of Health, U.S. Public Health Service.

In introducing this volume to English speaking scientists, it may be worthwhile to discuss briefly some aspects of the historical and philosophical background of the research described in this book. The accumulation of verifiable knowledge in the physicochemical and biological sciences during the nineteenth century exposed the inadequacies of the prevailing pseudoscholastic theories of medicine. Attempts were made to develop unified theories of medicine based on scientific principles and experimental data.

In western Europe and in the British Isles, under the impact of the Industrial Revolution and the mechanization of manufacturing processes, vitalism in biology was gradually being replaced by the philosophy of mechanism. In medicine this philosophy expressed itself in the cellular and localistic theory of disease, so eloquently formulated by one of its most distinguished proponents, Rudolf Virchow, in his monumental work *Cellular Pathology*. Disease was considered as due to the breakdown of specific tissues or organs in the same manner as the breakdown of a part of a man-made machine. Therapy was thought of primarily in terms of repair or restoration of the damaged tissue or organ.

This emphasis on organs, tissues and cells furthered the dissecting and analytic approach in the biological sciences and set the background for the development of detailed anatomic and physiologic investigations. It thus prepared the basis for scientific and rational diagnosis and therapy. This school of thought neglected, however, to give sufficient consideration to the integration of the living organism as a homeostatic, self-regulating unit, and to the importance of psychologic and other environmental factors.

In contrast, Russian biological and medical thinking, for a number of reasons which cannot be discussed here, remained little influenced by either vitalism or mechanism. It developed primarily on the basis of holistic and integrative concepts derived largely from some forms of philosophical materialism. This view was given its mature expression by Sergei Petrovich Botkin in clinical medicine and by Ivan M. Sechenov in physiology.

Briefly, Botkin and his followers postulated that, while all living processes, including psychic manifestations, can be ultimately analysed in terms of natural laws, they cannot be explained solely on the basis of the known laws of physics and chemistry. The characteristics of a biological unit (whether it be a single free-living protozoan or a higher metazoan) cannot be described in terms of the sum of the component elements of the organism any more than the properties of sulphuric acid can be described in terms of the sum of its component elements. This does not induce the chemist to resort to mysticism in explaining the properties of sulphuric acid or of a protein molecule. By the same token, the biologist need not invoke mystical vitalism to explain biological phenomena, including those associated with the activity of the cerebral cortex.

The kernel of this philosophic orientation consists of the concept of a hierarchy of levels of organization and configuration of matter in nature, each level of integration possessing qualities of its own. The quality referred to as life appeared at a certain level of organization of particular kinds of matter.

Living organisms exhibit a hierarchy of such levels of integration, beginning with integration within each cell and leading up to integration of organs and organ systems. The higher metazoan is integrated by the central nervous system, the cerebral cortex assuming a more dominant role in the higher mammals and reaching its acme in man. This dominant role of the cerebral mantle is maintained in relation to somatic as well as visceral functions and in the synthesis of these functions, so as to adapt the organism to its ever changing environment.

With the progressively increasing role of the cerebral cortex in the regulation of physiologic homeostasis in higher animals, especially in man, and the consequent increase in the multiplicity of physiologic responses to symbols of physico-chemical stimuli, there developed greater possibilities for the impingement of psychologic factors on various somatic and visceral functions. Botkin referred to this concept as the principle of "nervism", or the neurogenic theory of medicine. Ivan Petrovich Pavlov applied his genius to the experimental and theoretical amplification of this principle of nervism and thus established a new school of integrative physiology, at the same time laying the foundation for the scientific investigation of behavioral problems.

In this book Professor Asratian presents a summary of certain aspects of some two decades of research guided by the neurogenic theory and integrative concepts developed by the Botkin–Sechenov–Pavlov school. He obtained his physiological training in Pavlov's laboratories, after graduating from the Medical Faculty of Erevan University in the Armenian S.S.R. in 1930. In 1939 he was awarded the first prize of the U.S.S.R. Academy of Sciences and in 1950 the I. P. Pavlov prize.

In 1958 I had an opportunity to observe the work carried on in Dr. Asratian's laboratories when I was visiting the U.S.S.R. as a member of a cultural-scientific exchange delegation under the auspices of the American Friends Service Committee. I was very much impressed with Dr. Asratian's erudition, his enthusiasm for scientific inquiry, his friendly attitude and eagerness to share his scientific findings, and the meticulous care with which his experiments were planned and carried out. When the opportunity presented itself to prepare for publication an English translation of Dr. Asratian's book, I was glad to undertake this responsibility even though this involved a great deal of work on my part and took time away from my own research.

I was encouraged in this task by my good friend and colleague, Professor Chauncey D. Leake, and by my friend and mentor the late Professor John Farquhar Fulton, who had always been an admirer of Pavlov and who had a keen appreciation of the importance of the contributions of the Pavlov school to our understanding of the physiological basis of behavior. Grateful acknowledgement is also due to Professor W. Horsley Gantt whose writings and personal encouragement contributed greatly to arousing my interest in Pavlovian conditioned reflex studies and led me to undertake laboratory investigations in this exciting field of research. To Professors Benjamin Pasamanick and Ralph M. Patterson I wish to express my gratitude and appreciation for their continued support and encouragement and the provision of facilities for this survey and translation project.

I wish to take this opportunity to express my appreciation to Mr. Robert Maxwell of Pergamon Press for the confidence he placed in me by undertaking the publication of this series of translations and surveys. To my wife, Elizabeth O'Leary Corson, I wish to express my gratitude for lending her linguistic talents in finding just the right English equivalents for Russian scientific terms. During my trip to the U.S.S.R. and several consultations with Dr. Asratian at international scientific conferences, she not only kept the home fires burning, but also the Bunsen burners by undertaking the difficult task of directing the work in our laboratory. And last, but certainly not least, I wish to express my appreciation and sincere thanks to Mrs. Anne R. Coleman for her careful typing of the manuscript, her painstaking editorial assistance and proofreading, her scholarly tracking down of the multilingual bibliographic references and the application of her varied artistic, scientific and linguistic talents to the preparation of the figures for publication.

Ohio State University SAMUEL A. CORSON
Columbus, Ohio

AUTHOR'S PREFACE TO THE ENGLISH EDITION

THE author, together with his collaborators, has for many years conducted investigations dealing with basic problems of higher nervous functions and general neurophysiology which form the subject matter of this book. The first four chapters were published in Russian in 1959 by the U.S.S.R. Academy of Sciences, under the title *Lectures on Some Problems of Neurophysiology* and are based on a series of lectures delivered in several universities in Great Britain in 1957. Some important new data recently obtained by our laboratories were added to the English edition, particularly to the chapter devoted to the effects of cerebral decortication on neural and humoral functions. The two new chapters added to the English edition are based on material presented at the Symposium on Brain Mechanisms and Learning, held in Montevideo in 1959, and at the Pavlov Conference on Higher Nervous Functions, organized jointly by the New York Academy of Sciences and the Academy of Medical Sciences of the U.S.S.R. and held in New York City in 1960.

I should like to utilize this opportunity to express my gratitude to Pergamon Press for publishing my book in the English language and to Professor Samuel A. Corson for preparing the English edition for publication. I derive great satisfaction from the thought that the English edition of this book may help to strengthen the scientific contacts between scientists of different countries and thus serve in some measure the noble task of drawing together in mutual understanding the peoples of these countries, a task which so urgently needs to be accomplished in these troubled days.

E. A. ASRATIAN

AUTHOR'S PREFACE TO THE RUSSIAN EDITION

THIS book is based on a series of lectures delivered in November–December, 1957, in Great Britain, at the Institutes of Psychiatry and Neurology of the Univerity of London, the Physiological Institute of Oxford University, the Berden Neurological Institute in Bristol, the Medical School of the University of Birmingham, the Royal Society of Edinburgh, and the Medical Faculty of the University of Manchester.

These lectures summarize some of the data obtained by us and our collaborators on some basic problems of neurophysiology particularly related to spinal shock, compensation of functions, the influence of cerebral decortication on the neural and humoral regulation of functions of the organism, and on tonic conditioned reflexes. Although the subjects of these lectures appear to be different from each other, they are nevertheless interrelated and have been investigated by means of essentially similar physiological experiments: the utilization of radical neurosurgical procedures on animals and subsequent prolonged observation and experimental investigation of the results of these operations. Moreover, all of these investigations of ours have a common theoretical basis: the profound ideas developed by my teacher, I. P. Pavlov.

E. A. ASRATIAN

CHAPTER 1

THE PHYSIOLOGY OF SPINAL SHOCK

THE organs of the central nervous system of a highly developed organism react to a mechanical injury with a more or less protracted and profound suppression of the activity of those among their structures that have not been destroyed by the trauma. Spinal shock is a very significant and specific example of this phenomenon which is inherent in the entire central nervous system and perhaps attracts the attention of scientists more than any other. The importance of the experimental, clinical and theoretical study of spinal shock is also emphasized by the fact that the significance of progress achieved in this field invariably transcends the limits of this particular problem and finds a general application in the elucidation of numerous related phenomena of traumatic inhibition of functions in other central nervous organs.

Through his classic investigations on the physiology of spinal shock, the pioneer of neurophysiology, Charles Sherrington (1906), laid a firm foundation for further investigations in this direction and pointed the way to further progress in the study of this problem. Recent investigations of the phenomenon of spinal shock carried out by Liddell (1934), Fulton (1946), Forbes (1923), McCouch, Stewart and Hughes (1940, 1941), Van Rynberk and Ten-Cate (1939), Ruch (1942), Hinsey and Markee (1938) and others, actually continue these studies of Sherrington, further develop them experimentally and theoretically, and pinpoint and supplement some of his findings and ideas. Even many recent investigations concerning spinal shock which at first sight seem to have no connection with Sherrington's findings and ideas are, in the final analysis, bound up with them. Among such investigations are those of Harreveld (1940), Cannon and Rosenblueth (1949) and others.

The experimental material and concepts of Sherrington on this problem as well as the findings and tenets of my teacher, I. P. Pavlov, concerning some problems of the physiology and pathology of the nervous system, guided us and our co-workers in our investigations of the physiology of spinal shock, the main results of which I shall here describe.

The study of the problem of compensation, which we conducted over a period of several years and in the course of which we often resorted to the method of injuring the spinal cord by surgical means, aroused considerable interest in our laboratory in the physiology of spinal shock. At first we limited ourselves to accidental observations concerning the problem of spinal shock, but later we undertook a special experimental study of certain particular aspects of this problem which are of great theoretical as well as practical significance.

We now have some experimental material concerning the following three aspects of the physiology of spinal shock: (1) the causative factors; (2) the localization of the lesion in the central elements of the reflex arc in spinal shock; (3) the nature of spinal shock. The essence of this material and of the inferences derived from it is briefly as follows:

As is known, a series of new and well designed investigations have corroborated and developed Sherrington's proposition, according to which the development of spinal shock is determined by a disruption of the facilitating and intensifying influence of the suprasegmental central nervous organs on the nerve cells of the spinal cord. Whereas Sherrington originally believed that the source of this influence lay in certain nuclei situated in the area of the pons or of the midbrain, and was later inclined, together with his co-workers (Creed *et al.*, 1932), to believe that it lay in the bulbar nuclei, the experiments of Karplus and Kreidl (1914), and particularly those of Fulton and McCouch (1937), Fulton and Ferguson (1932) and others, have made it clear that in monkeys a still greater role in this respect is played by an intensifying influence which originates in the cerebral cortex and is transmitted along the corticospinal pathways. It should also be recalled that Sherrington and his pupils relied on a number of very definite findings when they supported their hypothesis that transection of the spinal cord evokes the phenomenon of spinal shock precisely because it interrupts the pathways along which this influence is transmitted, and when they rejected the idea of Goltz (1896) that traumatic irritation plays an important role in the genesis of spinal shock. Among the findings which confirmed Sherrington's view, the most important are the absence of the phenomenon of spinal shock in the cranial part of the transected spinal cord, and the fact that after a repeated transection of the caudal part of the spinal cord, which has emerged from the state of shock, the phenomenon of shock no longer develops in it. The findings which are the foundation of this essential hypothesis of Sherrington were subsequently confirmed by the results of Trendelenburg's experiments (1911) with the so-called cold transection of the spinal cord.

It may be said that the majority of current investigators adhere to Sherrington's views on this question. There are, however, some differing opinions, the essence of which must here be briefly described. Harreveld, for example, attributes the genesis of spinal shock to the existence of a specific spinal inhibitory structure or mechanism which is normally inactive, being under the inhibitory influence of the higher parts of the central nervous system. According to his opinion, the transection of the spinal cord evokes the phenomenon of spinal shock because it interrupts the pathways of the cerebral impulses which suppress this spinal inhibitory mechanism, and thereby gives an impetus to the activation of this mechanism, which in turn leads to suppression of the reflex activity of the spinal cord. Beritov's (1948) views on the development of spinal shock are to a certain degree similar to this hypothesis of Harreveld. Beritov also believes that it is the activation of a certain special structure of the spinal cord, its neuropile, which plays an important role in the genesis of spinal shock. In his opinion, however, the neuropile of the spinal cord becomes activated, not because it is freed from cerebral influences, but because of the mechanical stimulation caused by the transection of the spinal cord. Moreover, in agreement with Sherrington, Beritov concedes that interruption of the pathways which transmit the intensifying cerebral impulses to the cells of the spinal cord, as well as fatigue of the coordinating apparatus, also play an important role in the genesis of spinal shock. Rosenblueth tried to explain the process of emergence and disappearance of spinal shock by proceeding from Cannon's theoretical propositions concerning the heightened sensitivity of denervated structures (Cannon and Rosenblueth, 1949). Rosenblueth believes that transection of the spinal cord does not modify the normal condition and excitability of the nervous structures of its caudal part. As to the phenomenon of weakened reflex activity of this part which appears after the transection, this is due to the fact that the higher parts of the central nervous system can no longer participate in this activity nor exert any intensifying influence upon it. The subsequent intensification of reflex activity observed some time after the operation is regarded by Rosenblueth not as an indication of the restoration of the normal condition and functioning of the spinal neurons, but as an expression of their abnormally heightened excitability due to their specific denervation, i.e., degeneration of the descending pathways leading to the spinal neurons.

Whatever the difference may be among these opinions on the genesis of spinal shock, they are equally inadequate, since they are essentially speculative. The hypothesis concerning the existence of specific inhibitory mechanisms in the spinal cord, the activation of which is said to give rise to the phenomenon of spinal shock, like the hypothesis that transection of the spinal cord brings about no change in the functional condition of the cells of its caudal part, are not substantiated, directly or indirectly, by experimental material nor even by convincing theoretical arguments. It is characteristic of these opinions, in spite of their differences, that all derive to some degree from Sherrington's fundamental hypothesis concerning the significance of the interruption of cerebral impulses in the development of spinal shock; but each one changes and even distorts in its own way the meaning and essence of this hypothesis.

What is our own opinion on this question?

We have no doubt whatever as to the validity of Sherrington's basic hypothesis in its original meaning and essence, according to which the interruption of the pathways of suprasegmental facilitating and intensifying influences is a very important factor in the genesis of spinal shock. Definite data, however, which we have at our disposal provide a firm basis for stating that the role of this factor should not be overestimated, that the importance of traumatic irritation in the development of spinal shock should not be categorically denied, and that it is not quite valid to ascribe the phenomenon of spinal shock "exclusively", or "almost exclusively" (to use Sherrington's terminology), to the interruption of the pathways along which the influence of the suprasegmental formations is transmitted to the cells of the spinal cord.

What are the findings which we have in mind?

In the first place, we have often observed that in adult dogs a complete transection of the spinal cord, especially at the level of the last cervical or first thoracic vertebrae, does not limit itself solely to the development of shock in the caudal part of the spinal cord. There also occurs a marked suppression of the reflex activity of its cranial part, of the nuclei of the medulla oblongata and midbrain, and sometimes even of the higher cerebral organs. This is demonstrated by the observation that during the first days after the operation many animals exhibit a considerable weakening and even a complete loss of phonation, and that at the same time they are unable to straighten the fore part of the body, to support themselves on their forelegs, or to move with their help as they did at a later period (experiments of Drozdova and myself). Experiments performed on rabbits by Keder-Stepanova revealed definite changes in the bulbar respiratory centre even after transection of the spinal cord at the level of the last thoracic vertebrae. In the course of focal stimulation of the expiratory component of this centre by means of microelectrodes, the frequencies of the impulse current which evokes the inhibition of the inspiratory component of the centre decrease considerably as compared with the normal level. This is graphically shown in the pneumograms (Fig. 1). The suppression of the reflex activity of the bulbar nervous forma-

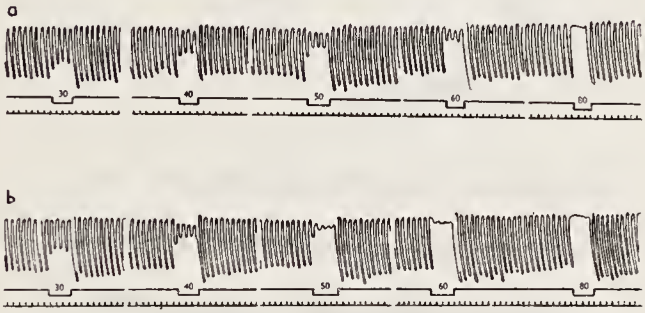

FIG. 1. Changes in the interpleural pressure in rabbits in response to unipolar focal stimulation of the expiratory structures of the bulbar respiratory centre by electric currents of various frequencies before (a) and after (b) transection of the spinal cord at the level of the inferior thoracic segments. From top to bottom: pneumogram; line of stimulation and of frequency of impulses per sec; time line in sec.

tions, as well as of the higher central nervous formations, is of a still more pronounced character when the spinal cord is partially transected at a higher level, at the level of the first cervical segments (experiments of Ivanova, 1956, Maksimova, 1956, and myself). For example, according to the experiments performed by Maksimova

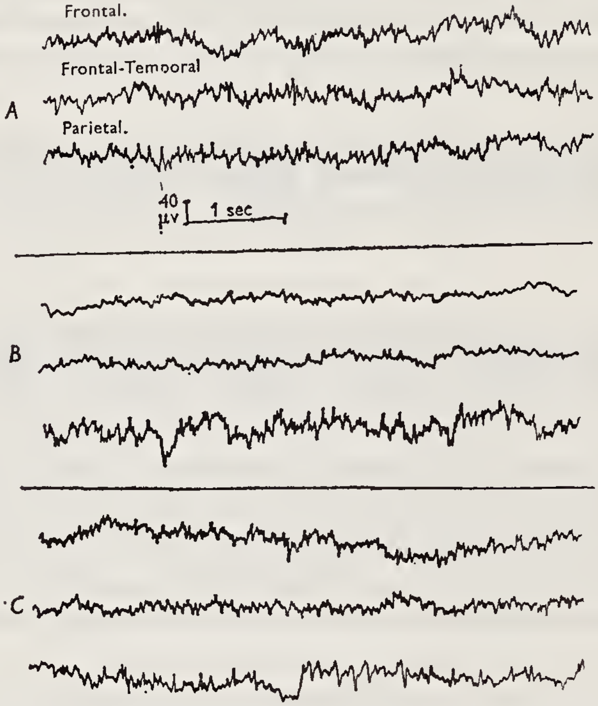

FIG. 2. Electroencephalogram of a dog before transection of the spinal cord (A), 2 hr after transection of the spinal cord at the level of the first thoracic segments (B), and one day after the operation (C).

on dogs and ducks, after a lateral hemisection of the spinal cord at the level of the second cervical segment, the electroencephalogram of the opposite hemisphere often proves to be suppressed for several days and then gradually returns to its initial level (Fig. 2).

The influence of the transection of the spinal cord on the functional condition of the cranial part of the spinal cord, the medulla oblongata, the midbrain and some other cerebral organs, is also confirmed by our data obtained by isotope methods (experiments of Musalov, 1955). The spinal cord of adult dogs was transected at the level of the sixth or seventh thoracic segment. After this operation (within periods ranging from several hours to two weeks) the following experiments were carried out on different dogs. Radioactive bromide or radioactive calcium were administered subcutaneously to the dogs (on the basis of 5000 impulses per g of body weight per min); one hour later, the dogs were killed by means of electric shock; then pieces were taken of the lower and upper segments of the spinal cord, of separate organs of the brain, and also in some cases of other organs, and after appropriate treatment the concentration of radioactive elements in them was determined. A comparison of the distribution of these elements in the various central and peripheral organs of intact control dogs and dogs whose spinal cord had been transected at different periods after the operation, gave an adequate basis for evaluating the changes which take place in their functional condition as a result of the transection of the spinal cord. Data obtained from experimentation on many dogs showed that after transection of the spinal cord the absorption of radioactive calcium deviates from the normal level not only in the caudal part of the spinal cord, but also in its cranial part, as well as in the cerebral organs, especially in the medulla oblongata, the cerebellum and the cerebrum. The extent and the dynamics of the changes

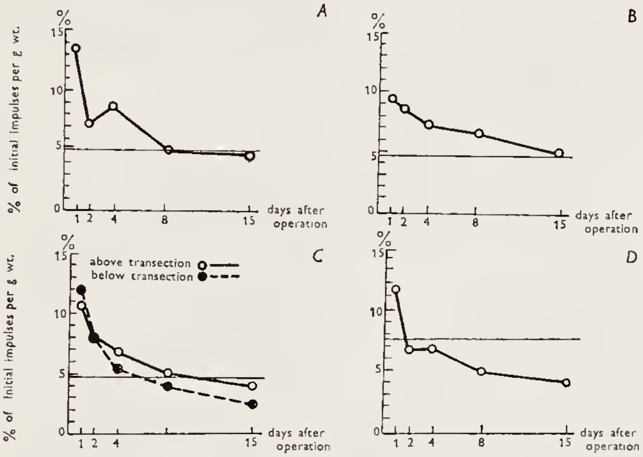

FIG. 3. Content of radioactive bromide in the cerebellum (A), cerebrum (B), spinal cord (C) and medulla oblongata (D) in intact animals and in animals with a transected spinal cord on different days after the operation. Horizontal lines indicate average values for normal animals.

which take place at different intervals after the transection of the spinal cord are shown in the diagrams (Figs. 3 and 4). From these diagrams we can see that the greatest changes in the absorption of radioactive bromide and radioactive calcium by these organs are

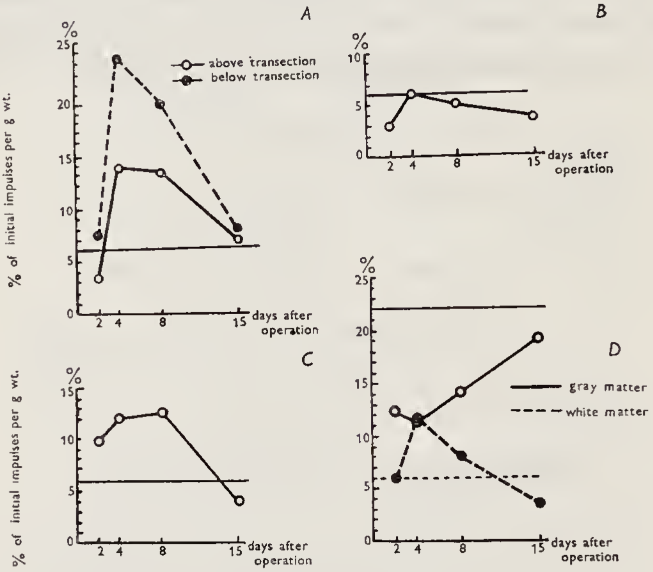

FIG. 4. Content of radioactive calcium in the spinal cord (A), medulla oblongata (B), cerebellum (C), and cerebrum (D) in intact animals and in animals with a transected spinal cord on different days after the operation. Horizontal line indicates average values for normal animals.

observed in the first postoperative days, i.e. at the stage of the most profound spinal shock; later these changes gradually diminish, and after a period of 7–15 days the organs under investigation return to normal in this respect. Only in those parts of the spinal cord which lie above and below the line of transection and directly adjoin this line, do these changes persist and remain clearly apparent even 15 days after the spinal operation (Fig. 5). It should be pointed out that the amount of radioactive calcium absorbed by these parts of the spinal cord is several times greater than that absorbed by the parts which lie far from the line of transection in either direction.

According to the above diagrams, these changes originally consist in an increased concentration of the radioactive preparations in both parts of the spinal cord as well as in the cerebellum and the cerebrum, and later in a gradual return of the concentration to its normal level or sometimes a decrease to below this level. Given these general characteristics, there are some differences in the rate and extent of the changes which take place in the various organs.

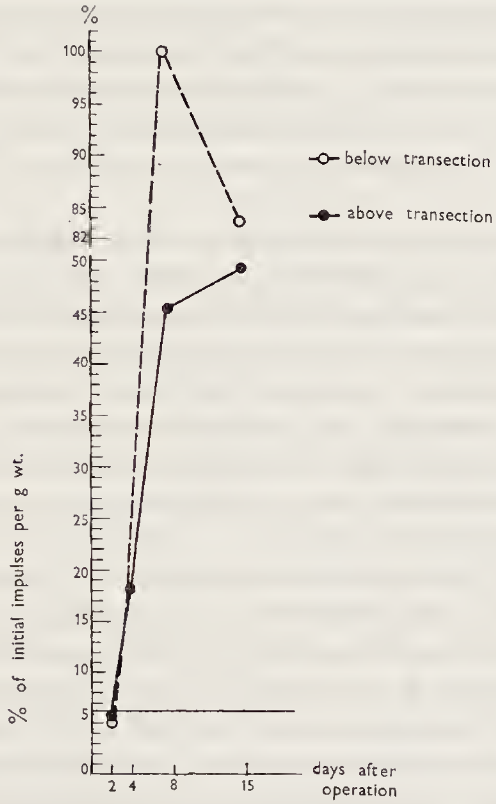

FIG. 5. Content of radioactive calcium in the segments of the spinal cord situated directly above and below the line of transection. Horizontal line indicates average values for normal animals.

These changes in the medulla oblongata are of a somewhat different kind. Here the absorption of radioactive bromide and calcium diminished, though not to a great degree, after transection of the spinal cord. Thus, after transection the relation of the cranial and caudal parts of the spinal cord, as well as of certain cerebral organs to the two neurotropic preparations which were administered, becomes considerably modified especially during the period of maximum intensity of spinal shock.

From all these findings it appears, then, that in highly developed organisms the transection of the spinal cord causes changes in many (if not all) organs of the central nervous system. This is by no means surprising since the spinal cord is in close connection and interaction with all parts of the central nervous system, and since surgical transection with its various consequences (mechanical action, disturbance of the circulation of the blood and of the cerebrospinal fluid, oedema and swelling, inflammation, toxaemia, degenerative changes, etc.) is a very serious and diversely acting trauma to the spinal cord which can alter its functional state profoundly and for long periods.

It should be noted that the degree of absorption of the above-mentioned radioactive elements by many peripheral organs and tissues which are innervated by the cranial part of the spinal cord and medulla oblongata as well as by the caudal part of the spinal cord, also changes as compared with the normal. This change, indicating an extensive and profound influence of the traumatic lesion of the spinal cord on the organism, gradually diminishes and subsequently disappears, just as this occurs in the organs of the central nervous system itself.

All the above findings, taken as a whole, give us an adequate basis for the following proposition: *A surgical transection of the spinal cord evokes the phenomenon of spinal shock in its caudal part and to a lesser degree in its cranial part, not only because it interrupts the cerebrospinal pathways which transmit the facilitating impulses to its cells, but also because it serves as a complex and long-acting traumatic stimulus which can alter the condition of both segments of the spinal cord and to some degree even the condition of the entire central nervous system.* As to the far greater intensity of spinal shock in the caudal part of the spinal cord as compared to that in the cranial part, this is caused by the fact that whereas in the caudal part there are two contributory factors, the disruption of the flow of facilitating impulses, which is the main factor, and the traumatic stimulus, which is subsidiary, in the cranial part only the latter factor is active.

We may also refer to some previously known data which were confirmed by our observations and which show that traumatic stimulation plays a certain role in the development of spinal shock. First we have in mind the definite dependence of the intensity and duration of spinal shock arising in the caudal part of the spinal cord on the completeness with which the surgical transection of the spinal cord has been made, on the proximity of the segments of the spinal cord to the area of transection, on the postoperative condition of this area, etc.

Further, we may also refer to the results of a repeated transection of the caudal part of a previously transected spinal cord, i.e. to those results which were used by Sherrington as an argument in support of his view on the genesis of spinal shock as against that of Goltz. It is, indeed, a well known fact that after such a repeated transection the phenomenon of shock recurs in the caudal end of the spinal cord, although it is of shorter duration and of considerably less intensity than after the first transection. This fact refutes Goltz's view, according to which traumatic stimulation is the one main cause of spinal shock. It does not, however, confirm Sherrington's view that traumatic stimulation bears no relation to the development of spinal shock. In this connection one well known observation must be mentioned which indicates the influence of transection of the spinal cord on the functional state of its cranial part. We have in mind the observation which was early described by Schiff (1858) and later by Sherrington (1898), and was recently elaborated by Ruch and Watts (1934). This is the phenomenon of intensification of the extensor reflexes and suppression of the flexor reflexes in the forelimbs after surgical transection of the spinal cord as well as after its novocain blockade at the level of the thoracic segments.

The second question which we must consider, the question of the localization of functions in the elements of the reflex arc under conditions of spinal shock, is one of the most important and complex questions in the entire problem. There is no doubt that modern neurophysiology will obtain more exact and valuable results in this area by means of the microelectrode method which makes it possible to establish separately the condition and activity of individual links of the central part of the reflex arc, as well as to stimulate them selectively. This does not mean, however, that other so-called old and considerably less exact methods of neurophysiological investigation must no longer be utilized in the study of this problem, as well as of other neurophysiological problems in general. Nobody will claim, for example, that the invention of a highly sensitive analytical balance has in any way abolished the necessity of using the "old," cruder type of balance, which is far less accurate but which permits the weighing of a considerably greater load.

I may remind you that Sherrington's view on the question of localization of the lesion of the elements of the reflex arc was not unchanged. Originally he believed spinal shock to be accompanied by "a loosening of nexus between the links of the nervous chain composing the arc; a defect of transmission at the synapsis" (1906, p. 245). He emphasized the close agreement of his point of view with that of Monakov, according to which the phenomenon of "diaschisis" is determined by the disfunction of the internuncial cells, "schaltzellen". Later Sherrington and his pupils departed to some degree from this original point of view and were inclined to accept the theory that it is the motoneurons which are most affected in spinal shock. They believed that in higher animals the transectioy of the spinal cord at first entails a complete decline in the activitn of the motoneurons; they explained this phenomenon by the fact that the spinal effectors are without the support of the higher parts of the brain and because of this are incapable of the activity which they carry out in lower animals (Creed *et al.*, p. 156). They supported this hypothesis by data obtained from the cytological investigation of chromatolytic changes which take place in the motoneurons of the caudal end of the transected spinal cord. Sorokhtin (1949), who took as a basis his own data concerning the antagonistic action of eserine to the development of spinal shock, also came to the conclusion that spinal shock atonifies the spinal motoneurons because the transection of the spinal cord leads to an interruption in the flow of supraspinal impulses and to a decline in the production of synaptic acetylcholine.

However, the subsequent thorough investigations by Liddell, as well as by Stewart, Hughes and McCouch, led to the conclusion that in conditions of spinal shock the functions of both the internuncial cells and the motoneurons are suppressed, which is manifested differently in animals of different levels of development. For example, according to the data of the three last-named investigators, who in their experiments utilized the electrophysiological method for recording the potentials of the spinal cord, the phenomenon of spinal shock in cats and dogs consists in the depression of the internuncial cells, while in monkeys the depression of the motoneurons greatly exceeds that of the internuncial neurons.

We also obtained some experimental data which, together with the above data of other investigators, make possible a better approach to this question. We have in mind the following concrete findings: As early as 1940, we performed in dogs transections of the dorsal half of the spinal cord at different levels for the purpose of studying some aspects of the problem of compensation; simultaneously we observed an interesting phenomenon which greatly surprised us at that time and which later became the subject of our special study. In adult dogs a very profound and protracted spinal shock as a rule develops below the line of transection, and this is of an even more pronounced character than a shock occurring after complete transection of the spinal cord. Of still greater interest and scientific importance are some other peculiarities of spinal shock which are caused by a dorsal hemisection. If, for example, such a hemisection has been made at the level of the middle or last thoracic segment, the reflex activities of the hind extremities, tail and pelvic organs often become suppressed to such a degree that during several postoperative days even strong tactile and nociceptive stimulations can produce no appreciable reflex reactions of these organs, nor any general or local reactions of the organs that are situated above the level of hemisection. At the same time the stimulation of the cerebral receptors in these animals (stroking the head, presenting food, saying their names, etc.) evokes a reaction not only of the fore extremities and head, but also of the hind extremities and tail. Although almost completely paralysed, these organs react to the natural stimulation of the cerebral receptors with lively movements.

This finding, which was established by us and verified and corroborated by Durmish'ian (1955) and some other scientists in our country, is of interest to us from three aspects. In the first place, it is not in accord with the results of the experiments performed by Fulton, Liddell and Rioch (1930). In acute experiments on cats they transected dorsally more than half of the diameter of the spinal cord, and that this transection did not lead to spinal shock was demonstrated, according to them, by the presence of the knee reflex. This considerable difference between the results of two related types of lesions of the spinal cord is apparently determined by different conditions in acute and chronic experiments and by different criteria for evaluating the condition of spinal shock, as well as by the peculiarities of spinal shock as developed in dogs and in cats, which have been noted by many investigators. In any case, we never observed any typical profound spinal shock in cats even after a full transection of the spinal cord. Sometimes immediately after the transection the spinal reflexes of the caudal part of the spinal cord are not suppressed at all but are, on the contrary, intensified.

In the second place, after transection of the dorsal half of the spinal cord, just as after its complete transection, spinal shock develops not only in its caudal part but to a lesser degree also in its cranial part, as well as in certain organs of the brain; this is demonstrated by a marked suppression of their reflex activity. This phenomenon is particularly pronounced when the transection is performed at the level of the cervical segments, especially the superior cervicals. In all probability, the structural foundation and mechanism of development of spinal shock after dorsal hemisection of the spinal cord are essentially the same as after its complete transection. In the case of dorsal hemisection part of the descending cerebrospinal pathways, and particularly the lateral corticospinal tracts, are transected. Moreover, a complex and protracted traumatic stimulation acts in both directions from the line of transection. It is possible that after a dorsal hemisection of the spinal cord, as well as after lateral and central hemisections, a definite role in the development of spinal shock is played by another, additional factor reported by Sechenov (1866) almost a century ago. This is the possible suppression of reflex activity by the higher parts of the central nervous system, which is effected reflexly through the medium of the intact half of the spinal cord and which is determined by the traumatic stimulation of the cranial parts of its transected ascending pathways.*

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*Although reflex influence of this kind may play some role in the genesis of spinal shock after incomplete transections of the spinal cord, the theory of Durmish'ian that precisely this mechanism is also responsible for the development of spinal shock after complete transections of the spinal cord seems quite improbable. Some of our experiments demonstrated that a complete transection of the spinal cord in adult dogs at the level of the last thoracic segments also entailed the development of spinal shock in the caudal part when, long before this transection, we performed in the animals a bilateral extirpation of the abdominal sympathetic chains, i.e. of the only pathways along which the influence of the cranial part of the central nervous system on its caudal part can be reflexly transmitted. Thus, the theory that this influence is instantaneously effected in

In the third place, this finding is of particular importance and special interest from the point of view of our question concerning the localization of the lesion in the elements of the reflex arcs under conditions of spinal shock. The possibility of activating the lower extremities and tail by the stimulation of the cerebral receptors indicates the fact that the absence of any reaction of these organs to the stimulation of their own cutaneous receptors is by no means determined by the disfunction of the motoneurons, but mainly by the withdrawal of the transmission to them of impulses along the segmental reflex arcs.

The results of our other experiments led us to a similar conclusion. The following interesting experiments were carried out by Drozdova on a number of adult dogs in which the spinal cord was completely transected at the level of the eighth to the tenth thoracic segments. In the state of profound spinal shock, when it is practically impossible to evoke either the extensor reflex of the hind extremities or the movement of the tail by intensive mechanical, thermal or electric stimulation of their receptive fields, these reflexes and movements can be evoked by moderate mechanical, thermal and electric stimulation of relatively unrelated receptive fields such as the areas of the anus, vagina and loins (Figs. 6 and 7).

Similar results were also obtained by Drozdova on a number of adult cats, in which the spinal cord was transected at the level of the middle thoracic segments. Since the reflex activity of the extremities is not suppressed in cats even during the most profound state of spinal shock, in the course of experimentation with these animals the attention of the experimenter was centered on the reflex activity of the tail which is suppressed to a considerably greater degree. The experiments showed that, whereas in the state of profound spinal shock it is impossible to evoke reflex movements of the tail even when it is subjected to strong mechanical, thermal or electric stimulation, such movements can be quite easily evoked by a moderate mechanical, thermal or electric stimulation of the areas of the anus, vagina, loins, and even of the limbs (Fig. 8).

the course of transection of the spinal cord and by means of those of its descending pathways which are transected one second or a few tenths of a second later than others, remains fully unsubstantiated and is essentially arbitrary.

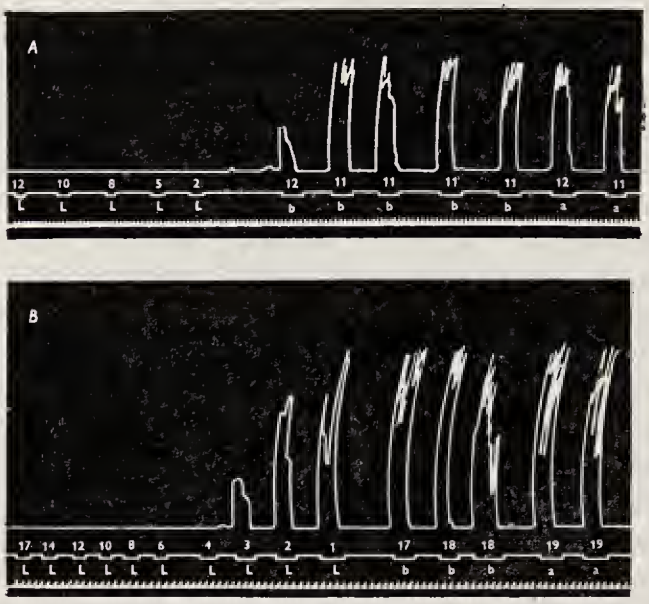

Fig. 6. Kymograms of the extensor reflex of a hind extremity in spinal dogs: (A) in dog "Kukla" on the fourth postoperative day; (B) in dog "Lissa" on the third postoperative day. The upper line indicates the reflexes; the middle line indicates the stimulations effected by means of induction current (the figures above denote the distance between the coils in cm and the symbols below denote the parts subjected to stimulation: L = hind limbs, b = vagina, a = anus). The lower line indicates the time in sec.

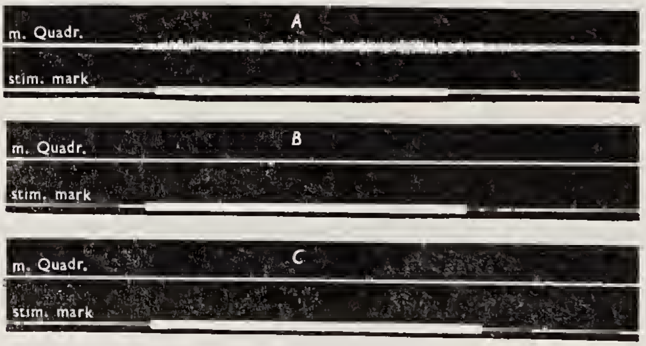

Fig. 7. Electromyogram of m. quadriceps in a spinal dog on the third day after transection of the spinal cord: (A) during mechanical stimulation of the region of the anus; (B) during mechanical stimulation of the paw of the same leg; (C) during mechanical stimulation of the contralateral extremity.

The following observations are also quite characteristic. In both dogs and cats the above phenomenon is particularly pronounced during the period when the spinal shock is of greatest intensity, i.e. during the first postoperative days. With the lapse of time, as the phenomenon of spinal shock gradually diminishes and the reflex activity of the hind extremities and tail reappear and become intensified under the stimulation of their adequate receptive fields, the above phenomenon, i.e. the reflex contraction of these organs as a result of the stimulation of some other, inadequate receptive fields, in most cases gradually declines and disappears. Thus, certain contrasting reciprocal relationships exist between these two groups of receptive fields which evoke reflex reactions of the limbs and tail.

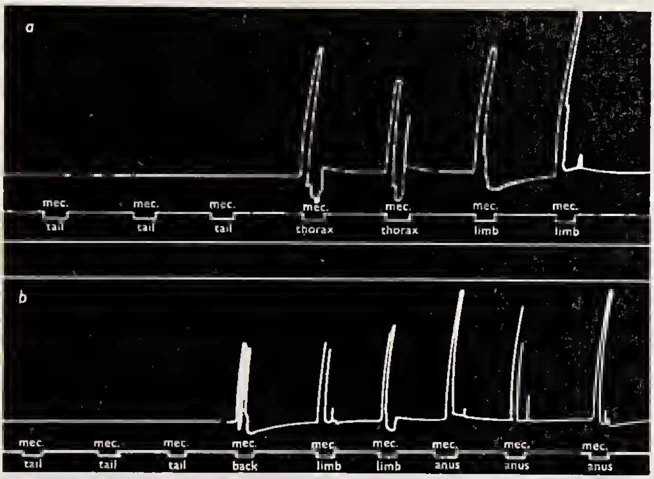

FIG. 8. Kymogram of reflex contractions of the tail in two spinal cats on the third (a) and on the second (b) day after the operation. The upper line indicates the reflexes, the lower line indicates the mechanical stimulation of the tail, extremity and anus.

It must also be pointed out that the motor reflexes of the limbs and tail which are evoked by the stimulation of the "inadequate" receptive fields do not show any particular stability, even during the period of the strongest manifestation of the above-described phenomenon. When a certain point of an inadequate receptive field is repeatedly stimulated, even at intervals of 3–4 min, the reflex weakens and disappears, almost as though it were fatigued. If adjoining points of the same receptive field or of some other inadequate field are then immediately stimulated, the same reflex appears in full strength. The phenomenon also exhibits certain individual variations: in some animals it is easily evoked in the region of the anus, in others in the region of the vagina, and in still others in the region of the loins. It may also be that the extensor reflex of the extremity of the animal is evoked by stimulation of the vagina and movement of the tail by stimulation of the anus, while direct stimulation of the extremities or of the tail does not produce in them any motor reactions whatever (Fig. 9). Moreover, during the period of profound shock when it is impossible by the stimulation of adequate receptive zones to evoke an extensor reflex in dogs and movement of the tail in cats, so-called spontaneous movements of these organs are often observed; they are apparently caused by certain humoral substances or other elusive internal or external factors.

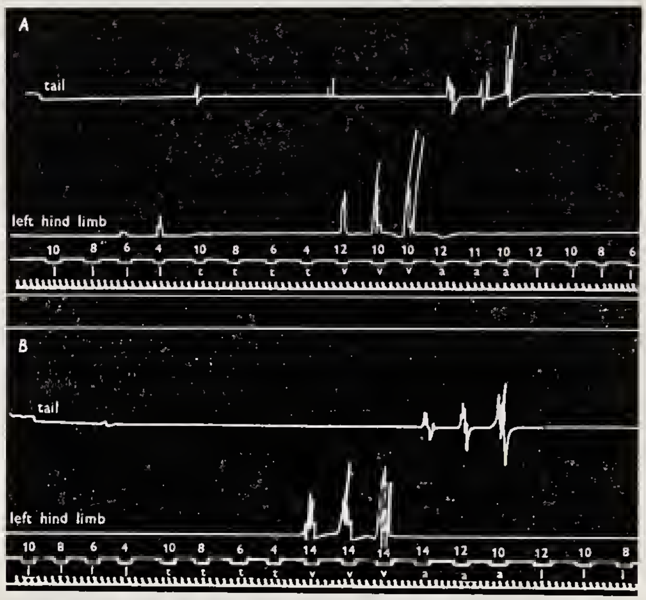

FIG. 9. Kymogram of the extensor reflex of a hind extremity and of the reflex movements of the tail in spinal dogs, (A) in dog "Mushka" on the second day after the operation, (B) in dog "Kroshka" on the third day after the operation, in response to stimulation by induction current of the limbs (1), tail (t), vagina (v) and anus (a).

It must be pointed out that the above phenomenon differs essentially from that described by Kocher (1896) in spinal patients and subsequently by many other clinicians, especially Kuhn (1950). Our investigation concerns the possibility of evoking in animals at the stage of profound spinal shock an extensor reflex of the hind limbs as well as movements of the tail through stimulation of the regions of anus, vagina or loins. As to the observations of the above-named clinicans, some report the preservation, in individual patients in a state of profound spinal shock, of genital reflexes evoked by stimulation of the genital organs or perineum, while others report that these reflexes recover first as the phenomenon of shock diminishes with the lapse of time. Subsequently, when the flexor reflexes of the lower limbs also recover, the stimulation of the genital organs and perineum begins to evoke flexor reflexes as well. It is possible, however, that these two phenomena, although different, may essentially have something in common.

I shall not yield to the temptation of considering here in detail the causes, origin, biological significance and other aspects of this phenomenon with all its various manifestations. This would only divert us from our immediate subject. However, regardless of the possible explanation of this phenomenon as a whole, all the above observations lead us to the same conclusion concerning the localization of the lesion in the elements of the reflex arc. The disappearance of the extensor reflex of the hind extremities in dogs and of the reflex movements of the tail in cats under conditions of profound spinal shock *depends only to a slight degree on the changes which take place in the functional state of the motoneurons of the corresponding reflexes; it is mainly determined by the disfunction of the preceding links of the arcs, due to the disturbance in them of synaptic transmission.*

It is interesting to note the agreement of our basic observations and our major conclusions with the histologic data reported by Liddell, according to whom profound degenerative changes take place in all the nerve cells in the caudal end of the transected spinal cord, with the exception of the ventral horns.

In a series of acute experiments on dogs Drozdova also studied the state of vasomotor reflexes in conditions of spinal shock. The data obtained from these experiments are in full accord with the results of her experiments described above, as well as with the previously described results of our experiments on dogs in which we transected the dorsal half of the spinal cord.

It was demonstrated by Claude Bernard (1859) that the transection of the spinal cord in mammals at the level of the last cervical or first thoracic segments causes a marked and stable decrease in the arterial pressure. As shown by the experiments of Bezold (1863), there also occurs a disappearance of the vasomotor reflexes following stimulation of the nerves which are connected with the caudal part of the spinal cord. However, Ludwig and Thiry (1864) demonstrated that under conditions of such experiments it is possible to raise the arterial pressure considerably by electric stimulation of the cross-section of the caudal segment of the spinal cord. These observations of the past were later repeatedly reproduced in the experiments of many scientists and studied by them from different aspects. Drozdova also performed such experiments and, having slightly improved the technique of stimulation, she obtained some new data regarding our problem. In the course of these experiments Drozdova stimulated separately various areas of the cross-section of the caudal part of the transected spinal cord as well as the sciatic nerve of the animals. For this purpose she used very thin bipolar electrodes completely covered (except at the ends) with insulating varnish and applied an electric current of moderate intensity. While the stimulation of the zones of the anterior and posterior columns, as well as of the sciatic nerve, did not cause any marked changes in arterial pressure, the stimulation of the zone of the lateral columns, i.e. the zone of greatest localization of the cerebrospinal sympathetic pathways and of the processes of the internuncial neurons, led to a rise in arterial pressure. We here present sections of kymograms from two such experiments, which show graphically the difference in the effects obtained from separate stimulations of various structures of the spinal cord in the state of profound spinal shock (Fig. 10). From the above data it follows that in spinal shock the efferent links of the arcs of vegetative reflexes, like those of the arcs of somatic reflexes, suffer considerably less than do the preceding links.

The nature of our experimental data does not permit us to determine precisely the degree of lesion of each link of the reflex arc in spinal shock. We believe, however, that these data sufficiently support our rough description of the severity of the lesion which affects these links in spinal shock; they also allow us to believe that the gradient of disfunction in spinal shock goes from the afferent to the efferent link of the reflex arc, and that it is the synaptic transmission between the afferent neuron and the first internuncial neuron which suffers the most.

Ten years ago when we first advanced this hypothesis, we could support it only by reference to well known laboratory and clinical

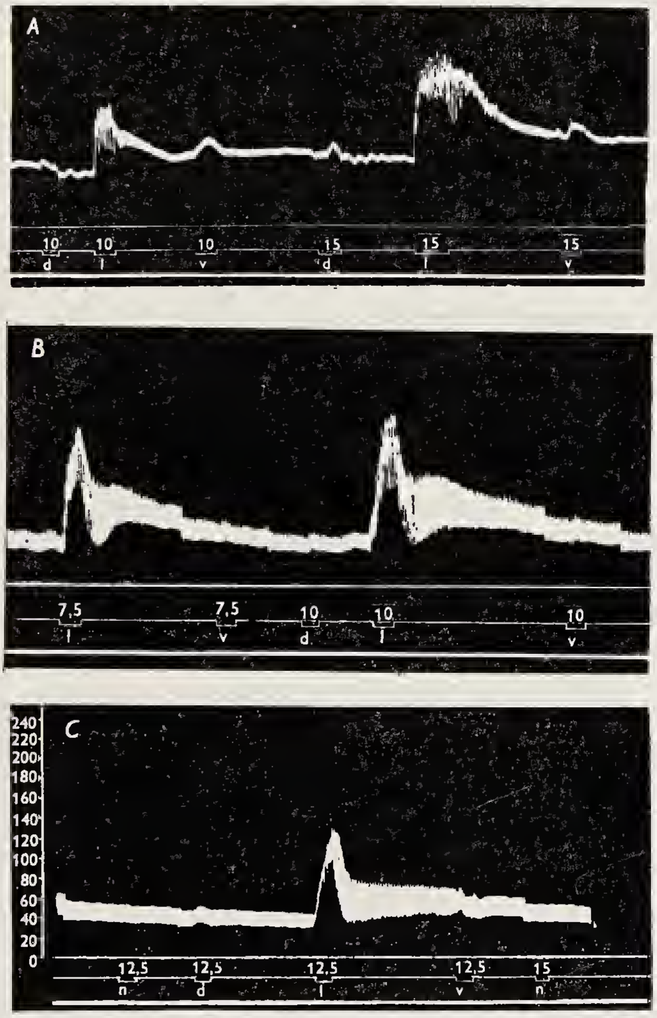

FIG. 10. Kymogram of arterial pressure in three spinal dogs during stimulation by induction current of different sections of the diameter of the caudal part of the spinal cord. From top to bottom: arterial pressure; line of zero pressure; line of stimulation. Above, distance between the coils in cm; below, stimulated section of transverse section of the spinal cord; l, lateral; v, ventral; d, dorsal; n, sciatic nerve; time in sec.

findings showing that the receptor functions of the organism are characterized by a particularly high sensitivity to many factors which in general tend to alter physiological functions such as fatigue, circulatory deficiency, hypoxia, wide fluctuations in temperature, various kinds of intoxication, general and local mechanical and other traumata, etc. At present there are many new exact and valuable data which, it seems to us, indirectly support the hypothesis that the afferent links of the reflex arcs especially are affected in spinal shock. We have in mind the following findings. In the first place, according to the data of Hagbarth and Kerr (1954), stimulation of the sensory motor zone of the cerebral cortex, of the reticular formation of the midbrain and of other cerebral organs, can exert an inhibitory influence on the synaptic transmission of sensory impulses in the first spinal afferent synapsis. On this basis we can state that a traumatic stimulation of the caudal parts of the transected cerebrospinal pathways which ensure this inhibitory influence, can cause the same effect and in the same link of the spinal reflex arcs. In the second place, and this is very important, there are many precise data showing that the transection of the processes of the nerve cells leads to profound and lasting changes in the structure of the damaged neurons and in their metabolism (Bodian and Mellors, 1945; Hyden, 1943). It also often evokes an appreciable and lasting suppression of their functional state and a temporary interruption of the synaptic transmission to them from preceding neurons, as well as the further transmission from them to subsequent neurons. These functional changes were demonstrated by Brown and Pascoe (1954) with regard particularly to the cells of the sympathetic ganglia and their presynaptic connections after transection of the postganglionic fibres; Dowman, Eccles and McIntyre (1953) demonstrated these functional changes in respect to the motoneurons as well as the monosynaptic reflexes which are connected with them, after transection of the axons of the motoneurons; Eccles and McIntyre (1953) did the same with respect to the neurons of the intervertebral ganglia and their monosynaptic connections after transection of the posterior routes in a distal direction from these ganglia.

Although the precise nature of this interesting phenomenon still remains obscure, it is probably caused by a trauma of the neurons, a stable and strong traumatic over-stimulation of the neurons resulting from the injury to their processes. If we take these facts into account (no matter how their mechanism and nature may be explained) and try to evaluate the possible consequences of the transection of the spinal cord on the nerve cells of its caudal part, we shall obtain the following picture. The motoneurons of this part will be affected mainly because of the interruption of the pathways along which the intensifying and facilitating cerebral impulses are transmitted to them; their processes, however, will remain undamaged. Most of the afferent neurons, however, will be affected mainly by the interruption of their central processes. Some of the internuncial neurons situated in either direction from the line of the transection will be affected for the same reason. All this is due to the particular spatial disposition of the motoneurons and of the internuncial and afferent nerve cells and their processes within the spinal cord, which is schematically represented in Fig. 11. From the above as well as from the diagram, it appears that the phenomenon of spinal shock in the caudal part must be of a more profound nature than in the cranial part, and that in both cases it reaches maximum intensity in the region of the transection, in the zone within which the collaterals of the internuncial neurons are primarily distributed above and below. We have already referred

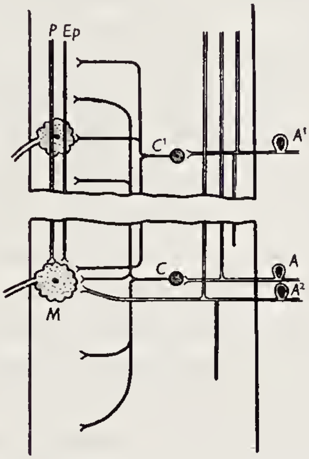

FIG. 11. Diagram illustrating injury of the processes of the basic neurons of the spinal cord as a result of its transverse section. M, motoneuron; C, C^1, internuncial neurons; A, A^1, A^2, spinal ganglia; P, pyramidal tract; Ep, extrapyramidal tract.

to some other factors relating to the damage of these nerve cells and of their synaptic connections after transection of the spinal cord, and there is no need to repeat these remarks.

All that has been said above helps us to understand the mechanism of shock in cases when only the dorsal half of the spinal cord is transected. Besides an interruption of the posterior corticospinal pathways, there also occurs an interruption of the main ascending afferent pathways as well as of the processes of some of the internuncial neurons.

It is obvious that our data and viewpoint concerning the question of localization of the lesion in the links of the reflex arc in spinal shock are largely in accord with Sherrington's original viewpoint as well as with the data and concepts of Liddell, McCouch, Stewart, Hughes, and others. But unlike these last investigators, we believe that in carnivorous animals not only the efferent and internuncial links of the reflex arc suffer in spinal shock, but also, and to an even greater degree, its afferent link. I admit, of course, that no matter how well this hypothesis may be substantiated by indirect evidence and considerations, it still needs direct experimental verification, and this we intend to provide in the near future.

It now remains only for me to say a few words concerning the third question, namely, the nature of spinal shock.

Unlike Goltz, who regarded the phenomenon of spinal shock as a state of protracted inhibition caused by traumatic stimulation, Sherrington thought that "the condition of the spinal reflex arcs in spinal shock appears to resemble a general spinal fatigue rather than an inhibition" (1906, p. 245). He reached this conclusion mainly from the fact that scratch and flexor reflexes in the period of spinal shock show some characteristic features of fatigue: irregular rhythm, sluggishness of separate contractions, rapid weakening of movements under repeated stimulations, etc. Clearly, this hypothesis of Sherrington is in full accord with his theory of the origin of spinal shock: the cells of the spinal cord are deprived of the flow of facilitating and intensifying cerebral impulses, and therefore they become weakened and easily fatigued.

It seems probable that in this as in many related neurophysiological questions, the complex relationships between the phenomena of fatigue and inhibition can be properly understood, not through their contraposition ("either—or"), but through their combination ("both – and"). An illustrative and convincing example of precisely such an approach to the relationship between fatigue and inhibition is Pavlov's theory of the protective role of inhibition, which is based on extensive experimental material concerning the normal and pathological activity of the cerebral hemispheres. This theory does not identify the phenomena of fatigue and inhibition in the nerve cells of the cortex, but on the other hand it does not oppose them to each other, or, to be more precise, it does not regard them as incompatible, mutually exclusive conditions. According to Pavlov, fatigue stimulates the development of inhibition in the cortical nerve cells and actually originates it.

As far as I can judge, the idea of the compatibility of the phenomenon of reflex fatigue with that of inhibition was not alien to Sherrington.

Since this theory of Pavlov not only served as a model for the correct solution of the complex problem of the interrelation between fatigue and inhibition, but also determined our approach to the understanding of the physiological nature of spinal shock, we shall digress somewhat from the subject at hand and describe briefly the essence of this theory.

According to Pavlov, inhibition is not only an important coordinating factor in the activity of the cerebral cortex, but it also plays another, no less important role, protecting the highly reactive and vulnerable cortical cells when their normal condition and normal activity are impaired or when they are in danger of disease or injury. In the course of the normal vital activity of the organism the development of such protective inhibition in the cortical cells of the cerebral hemispheres is due to two factors: either the action of an extremely strong stimulus for even a short period, or the prolonged action of a stimulus of moderate intensity. The extremely intensive excitation of the cells in the first case, and the greatly prolonged excitation in the second, bring about the same effect, namely, they fatigue and exhaust the cells, as a result of which inhibition develops which prevents such further fatigue and exhaustion of the cells as would threaten their normal activity. Pavlov wrote: "The ensuing inhibition, which in itself is not fatigue, appears in the role of a protector of the cell which prevents further excessive and dangerous destruction of this particular cell" (1947, p. 210). Moreover, being overcome by inhibition, the fatigued and exhausted nerve cells effectively restore their normal working capacity, as occurs, for example, in normal daily sleep which was regarded by Pavlov as a universal protective inhibition of the cerebral cells. As mentioned above, the fatigue and exhaustion of the cortical nerve cells is an essential condition for the emergence of protective inhibition; it is even an impetus to its development and is its stimulant.

According to Pavlov's theory, the inhibitory process in the cortical cells also appears as a natural measure of self-defence in those cases when, under the influence of certain pathogenic factors acting as unusual and very strong stimuli, the cortical cells become over-excited, fatigued, and so greatly exhausted that there results the development in them of a pathological condition. Unable to resist the pathogenic factor and to avert the emergence of a pathological condition in the cortical cells, the inhibitory process in such cases often plays the role of a "physiological measure" directed against the consequences of the action of this factor; it does not allow the pathological process to intensify and spread over the mass of the cortex and contributes to the healing and recovery of the latter. This property of inhibition was utilized by Pavlov for the theoretical support of experimental and clinical sleep therapy in a number of nervous and mental diseases.

Proceeding from the hypothesis that the basic laws of activity of numerous organs of the central nervous system have common roots as well as many common features, and basing our thinking on the results of special investigations (which need not now be discussed), we suggested that the area of application of this theory of Pavlov should be greatly extended. In developing his ideas, we believe that inhibition plays a protective and restorative role throughout the nervous system and in all of its central organs, both under conditions of normal activity and also in functional and organic pathological states. We have made an attempt to understand and interpret from this point of view the physiological essence of phenomena which take place in the disturbed central nervous system, such as central shock, diaschisis, reflex paresis and paralysis, depression of the activity of the nervous system as a result of traumatic shock, spinal shock, etc., which are usually regarded as isolated phenomena the nature and biological significance of which are not understood. Indeed, the aetiology of all these phenomena comprises the most essential factors and prerequisites for the genesis of protective and restorative inhibition, namely, the destructive stimulation which can greatly overstimulate the parts of the central nervous system which remain intact and evoke an extremely rapid fatigue and profound exhaustion of the nerve cells of these parts. Moreover, these phenomena alone have all the essential features of inhibition, which was long ago estabtlished by many investigators and characterized by them as an almost necessary evil which accompanies any trauma. Following Pavlov's viewpoint, we also believe that the phenomenon of inhibition in such conditions should be regarded as a measure of self defense and self treatment of the nervous structures which remain intact but are affected by the traumata.

In a number of cases we were able to verify this conclusion under conditions of laboratory experiments on animals. Our fundamental finding can be summarized as follows: a drug-induced sleep of moderate, so to speak "physiological" depth and duration produced by non-toxic soporifics contributes to the rapid recovery of animals suffering from various traumata of the organs of the central nervous system or of any other organs.

Applying to our specific subject what we have said concerning the protective and restorative role of inhibition, we can state that we regard the physiological nature of spinal shock mainly as a prolonged protective and restorative inhibition of the nerve cells of the spinal cord caused by some organic injury of its structure. This pathogenic factor particularly affects the aboral part of the spinal cord where it evokes a more profound and prolonged inhibition since, on the one hand, it interrupts the pathways of the beneficial cerebral influences on this part of the spinal cord and thus weakens it, and, on the other hand, it strongly stimulates the spinal cord anew. As to the cranial part of the spinal cord, the influence of this factor proves to be less pronounced because it acts only as a strong stimulus, and the intensity and duration of inhibition in this part are therefore less.

A special series of experiments performed by Drozdova revealed some of the characteristics of protective and restorative inhibition in the caudal part of the spinal cord under conditions of spinal shock; among them are: wave-like oscillations of the degree of reflex activity, some parabiotic phases, i.e. a lack of correlation between the strength of reflexes and the intensity of the stimuli, and in particular a marked reduction of the duration of spinal shock, i.e. an accelerated rate of recovery of somatic and vegetative reflexes under the influence of moderate doses of non-toxic soporifics. Figures 12 and 13 show this graphically regarding flexor reflexes of the hind limbs and vasomotor reflexes, as well as the reflex emptying of the urinary bladder. It is to be noted that after excessive dosages the beneficial effect of the soporifics decreases, disappears, and is often even replaced by a harmful effect. The beneficial effect

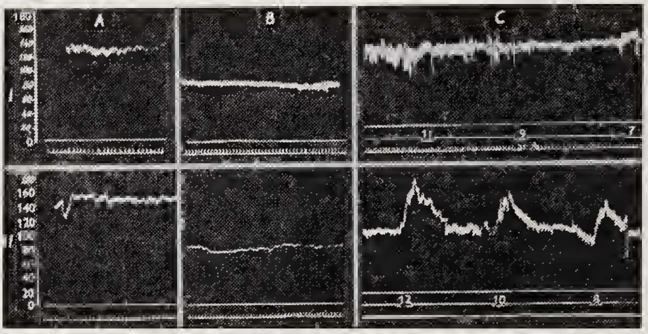

FIG. 12. Kymograms of arterial pressure in the control spinal dog "Pushinka" (I) and in spinal dog "Vydra" (II) subjected to sleep therapy: (A) before the operation; (B) two days after the transection of the spinal cord at the level of the first–second thoracic segment; (C) 35 days after the same operation. From top to bottom: arterial pressure; line of zero pressure; line of stimulation by induction current of the sciatic nerve; time in sec.

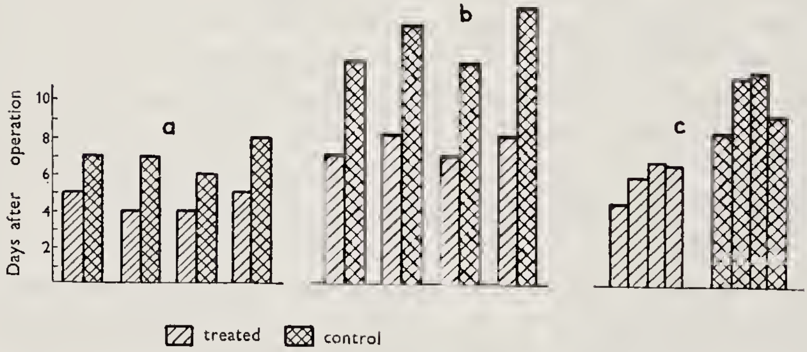

FIG. 13. Diagram illustrating the influences of drug-induced sleep on the rate of recovery of reflexes in spinal dogs: (a) flexor reflex of the hind extremities; (b) urination; (c) vasomotor reflexes.

of moderate doses of non-toxic soporific preparations was also observed in spinal shock caused by transections of the ventral, lateral or dorsal half of the spinal cord (experiments of Ivanova, Urgandzhian, 1953, and our own experiments). It is easy to see that the above viewpoint on the development of inhibition in conditions of spinal shock differs essentially regarding the structural foundation and mechanisms of development of this inhibition, as well as regarding the interpretation and evaluation of its significance, from the views of Goltz, Harreveld and Beritov.

This, in brief, is our principal experimental material and these are the resultant hypotheses concerning the three aspects of spinal shock mentioned above. For the sake of greater clarity, the experimental material and the hypotheses can be summarized under the following three points: (a) transection of the spinal cord evokes spinal shock not only in its caudal part, but to a lesser degree also in its cranial part and in certain organs of the brain. The significance of such transection is not confined to the interruption of the pathways of cerebral influences on the structures of the caudal part of the spinal cord, but it is also expressed to some degree in a complex, strong and protracted traumatic stimulation of the two separated parts of the central nervous system; (b) in spinal shock all the links of the central part of the reflex arcs become affected, i.e. not only the efferent and internuncial neurons, but also the afferent neurons of the arcs with their synaptic apparatuses, and the afferent links moreover become more profoundly affected than any others; (c) the physiological nature of spinal shock consists mainly in the development of protective and restorative inhibition within the elements of the central parts of the affected reflex arcs as a result of their overstimulation, weakening, fatigue and exhaustion.

In conclusion, I should like to emphasize once more that the modern theory of spinal shock was founded by the pioneer of neurophysiology, Sherrington, and that long ago in his initial investigations concerning the physiology of the spinal cord he skillfully outlined the correct solution of this complex problem which is of both scientific and practical importance. At present his pupils and followers in England, the United States and other countries succesfully carry on the investigation of this problem; they elaborate, refine, supplement, and sometimes even amend Sherrington's initial data and further develop his profound ideas.

We believe also that our above-described observations and hypotheses advance and develop Sherrington's initial data and ideas concerning the phenomenon of spinal shock, since in some respects they define, particularize and extend them, and in other respects supplement and amend them.

Having had the good fortune to be a pupil and follower of the great Pavlov, whose creative scientific activity has much in common with that of Sherrington (in spite of some basic differences in their views on certain questions of cerebral activity), I also felt the great influence of Sherrington on the formation of my views concerning the fundamental general problems of neurophysiology. Through our investigations we and our collaborators have pursued a definite goal: we have attempted to approach the study of certain aspects of the problem of spinal shock, which is a truly Sherringtonian problem, from the point of view of the ideas of our teacher Pavlov, i.e. properly speaking, in this respect to synthesize the fundamental ideas of these two giants of neurophysiology.

I must confess that I feel a kind of alarm at the thought of whether we have so far succeeded in attaining, even to some degree, this important and lofty aim.

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CHAPTER 2

THE ROLE OF THE BRAIN IN THE COMPENSATION OF FUNCTIONS

The problem of compensation of disturbed functions in among the most urgent problems of modern biology and medicine and is of great theoretical as well as practical importance. It is a well known fact that one of the characteristics of organic evolution is a progressive differentiation and specialization of structures and functions, a gradual weakening and even disppearance of the capacity to regenerate lost or injured organs or tissues and, along with this, the development of other predominantly functional means of restoring the disturbed or lost functions. This is a clear demonstration of adaptation, which is one of the cardinal attributes of living matter.

Physicians have long observed that after mechanical lesions in many external and internal organs in man, such as the arms, legs, digestive organs, kidneys, etc., there often occurs a marked recovery of the disturbed or lost functions, either by the compensatory use of the intact parts of the injured organ as well as of the corresponding synergetic organs, or by a compensatory readjustment of the functions of other organs. Later, with the development of physiological experimental research on animals, scientists began also to collect laboratory data which were identical with the above-described observations. In the nineteenth century, which was marked by a tremendous development of biological sciences and by the foundation of truly scientific physiology and medicine, clinical and laboratory work on the accumulation of observations concerning the restoration of disturbed and lost functions of an injured organism was conducted on a considerably larger scale, and, which is particularly important, at a higher scientific level than previously. This can be illustrated by a number of laboratory findings which were obtained in the nineteenth and the beginning of the twentieth centuries and which give evidence of an appreciable recovery of disturbed functions in animals after the removal of certain parts of the cerebral cortex (experiments of Luciani, Goltz, Ferrier, Tarkhanov, Hitzig, Schäfer, Horsley, Pavlov, Bekhterev, *et al*); after partial or complete removal of the cerebellum (experiments of Luciani, Van Rynberk, *et al.*); after various partial lesions of the structure of the spinal cord (experiments of Brown-Séguard, Sechenov, Weiss, Osawa, Rossolimo, Mott, Marshall, Bekhterev, *et al.*); after transection of separate stalks of the cerebrum or cerebellum (experiments of Goltz, Starlinger, Rothman, *et al.*); after deafferentation of the extremities or neck (experiments of Bickel, Munk, Baldi, Trendelenburg, Magnus, *et al.*); after transection and cross anastomosis of various nerves (experiments of Fluorens, Lengley, Mislavskii, Rawa, Bethe, Osborn, Kilvington, *et al.*); after amputation of the extremities (experiments of Fuld, Bethe, *et al.*); after transplantation of tendons of the skeletal muscles (experiments of Codivilla, Marina, Perthes, *et al.*); after destruction of the labyrinths (experiments of Ewald, Bekhterev, Magnus, *et al.*).

It should be pointed out that at this stage of its development research connected with the identification and description of the various phenomena of compensation did not yet have the character of planned and systematic investigation; it may even be said that many of the above-mentioned data were obtained incidentally in the course of studying quite different problems. Nevertheless, with the steady expansion of the range and diversity of clinical and experimental material of this kind, the general outlines of the problem as a whole became more and more distinct, and this eventually led to its formulation as an independent and important scientific and practical problem.

The study of this problem during the past 30–40 years has been characterized by a considerable growth in the number of special and systematic experimental investigations aimed at the solution of its more complex and more important questions, the formulation of the mechanisms and laws which govern the phenomena of compensation, a more exact definition of the role and significance of various internal and external factors in their development, etc. It was during this period that clinicians progressed from passive observation to active control of these phenomena, namely, the replacement of paralyzed nerves and muscles by other, normally functioning nerves and muscles, the creation of artificial motor organs, such as the Krukenberg "fingers," the elaboration and application of methods designed to activate the process of restoration of functions in patients suffering from lesions of various organs of the central nervous system, etc. A characteristic and essential feature of this new stage in the development of the study of compensation was the publication of the first summaries of the abundant but unorganized old and new data concerning different aspects of the problem. These summaries also made the first attempt theoretically to analyse and generalize this material from a definite point of view and to formulate the theory of the problem as a whole. I refer to the summaries of Bethe (1931), Bethe and Fisher (1931), Sperry (1945), Anokhin (1935), Asratian (1953), and others.

Many investigators of the problem of compensation have long held common views on some of its important aspects. These particularly concern the interpretation of the phenomenon of compensation in an injured organism as a specific adaptation of the organism to changed environmental conditions. It is generally assumed that these phenomena do not differ essentially from the various so-called compensatory adaptations which take place in a normal organism according to that individual's type of activity; like these adaptations they are chiefly effected by the nervous system according to its normal laws of activity.

However, since the views of physiologists on the general principles and laws of activity of the nervous system differ, their approaches to some of the fundamental questions of compensation also vary. This particularly concerns the question of the physiological mechanism of compensatory adaptations as well as the nature of their development, the question of the factors which determine their formation and accomplishment, the question of the relation of various parts of the central nervous system to compensatory adaptations, and finally the question of the characteristics of their development according to the evolutionary level of the given organism.

It should be pointed out that there are at present two basic trends which approach the solution of these questions in different ways. The adherents of the first trend oppose the reflex theory and attempt to interpret the phenomena of compensation in the light, one might say, of certain principles of the Gestalt theory; the adherents of the second trend approach the same phenomena from the point of view of the basic principles which underlie the reflex theory of the activity of the nervous system. The number of adherents of the first trend, which was founded by Bethe jointly with Fisher, Goldstein (1931), Holst (1934), and others, is now, apparently, quite small. Essentially their views are as follows: they believe that compensatory adaptations, or the change of coordination which underlies them, develop in the injured organism very rapidly and, as it were, automatically. According to Bethe, phenomena of compensation in an injured organism "are already present and are not learned by the trial method." They are determined by impulses coming from the receptors, which not only inform the central nervous system of the injury inflicted on the organism, but by their impulses actively form the necessary new kinds of coordination by means of an instantaneous readjustment of the functions of the corresponding parts of this system. Functionally, the central nervous system is represented as an amorphous network and is distinguished by its high plasticity; the accomplishment of this readjustment, just like the activity of the central nervous system in general, is fully controlled by the periphery, i.e. by the peripheral impulses. The process of readjustment takes place in the structures of the "primitive" (according to Bethe's terminology) parts of the central nervous system of the organism, while its higher parts, i.e. the organs of learning, here play no appreciable role or no role at all. According to Bethe, in invertebrates and lower vertebrates, as well as in birds, mammals and man, the development of compensatory adaptations is essentially similar; it is subject to the same laws, effected by the same mechanism, influenced by the same factors and has the same central localization.

Because of limitation of space, I am unable here to subject the views of Bethe and his adherents to a critical evaluation and shall therefore only point out that their views are insufficiently supported by reliable and convincing data. I refer, for example, to those data on the basis of which Bethe and his adherents firmly deny the participation of the higher parts of the central nervous system in the development of compensation in all living beings, irrespective of their evolutionary level, i.e. data which have a direct bearing on the present subject. They are as follows: neither the removal of the parapharyngeal nerve ganglia in the beetle *Dytiscus* nor the removal of the motor zones of the cerebral cortex in dogs causes the disappearance of the compensation which occurs after the amputation of certain extremities. In stupid animals (among which, according to Bethe and his followers, are guinea pigs) and in intelligent animals (among which, in their opinion, are dogs) the disturbed motor functions are restored at the same rate.

Bethe and his followers do not take into consideration, and do not even mention in their articles, the early, well known and far more numerous and convincing data concerning this problem which were obtained by many other investigators, and which, as we shall see later, support a diametrically opposite point of view. They show a similar tendentiousness in their selection of data in support of their other theories. They have, therefore, turned reality into their powerful enemy and at the same time into a reliable ally of their adversaries, the adherents of the reflex theory, who represent another trend in the investigation and interpretation of questions concerning the compensation of functions.

All the experimental and clinical data relating to the problem of compensation which were obtained by numerous scientists in the nineteenth and early twentieth centuries demonstrate the fact that after severe injury to the organism the compensatory adaptations as a rule develop gradually and often quite slowly by means of systematic training, which in higher animals clearly has the characteristics of learning. From these various observations it also follows that in different animals these adaptations differ in nature, dynamics, mechanisms, central localization and other characteristics, and that they depend to a considerable degree on the evolutionary level of the animals. An unbiased analysis of these abundant data shows that they fully accord with the principles of the reflex theory which was brought to its present high level of perfection by the work of the pioneers of neurophysiology, especially Sechenov, Sherrington, Pavlov and Magnus. Many phenomena of compensation can be easily and satisfactorily understood and explained if we take into consideration such characteristics of reflex activity as its dynamic character, variability, and high degree of adaptability which depends on a number of external and internal factors, especially on afferent impulses, i.e. if we take into consideration the characteristics which are to some degree inherent in all reflexes and are most highly developed in conditioned reflexes. The comprehension and explanation of the essence of the highly diverse phenomena of compensation will be even more complete if we also take into account characteristics of the central nervous system which develop in the course of evolution, such as its functional specialization, the specific character of the reflex activity of its various organs, the functional hierarchy of these interacting organs within the system, which is directed by the cerebral cortex in higher animals and man, and the encephalization of the functions of the organism.

Under these conditions does it not seem historically paradoxical that in the area of such an important and urgent problem as that of compensation, there was for a long time no definite scientific tendency among the adherants of the reflex theory to propose a unified approach to all the fundamental aspects of this problem? Moreover, not only was this problem not studied in a systematic and planned manner from the point of view of the reflex theory, but until recently no attempts were even made to summarize, generalize and elucidate in the light of this theory the abundant empirical material relating to this problem which had been accumulated by numerous physiologists and physicians over many decades, largely in the course of studying other problems. It is this weak position of the reflex theory in the experimental and theoretical investigation of the probelm of compensation which is, apparently, responsible for the rapidly growing influence, and even temporary domination, of the above-mentioned more organized and defined trend of Bethe and his followers.

There is good reason to believe that the situation in this field has recently changed markedly in favor of the adherents of the reflex theory. This change was brought about by the joint efforts of many scientists who support the reflex theory of nervous activity. We and our co-workers in particular were among the first to undertake such a systematic and planned investigation of the problem of compensation from the point of view of the reflex theory, and have been engaged in this research for 25 years.

In criticizing in our publications the theories of the opponents of the reflex theory, in arguing against their views on certain aspects of the problem of compensation and in defending the principles of the reflex theory in this connection, we rely not only on data obtained by us and other modern scientists; we also always make use of many valuable early observations concerning this problem, most of which have been almost entirely forgotten and which we have now discovered in the early literature. It is impossible to dwell here even briefly on this varied and rich material, and I must confine myself to a short description of the data which are now at our disposal and which concern the role of the higher parts of the central nervous system in the phenomena of compensation which occur after injury to other organs of this system or to the peripheral receptor and effector organs and nerves.

As far back as the end of the last century and the beginning of this, many scientists, mainly physiologists, performed numerous experiments on animals: first, by means of surgical operations, they injured certain peripheral or central organs or nervous conductors and then, after restoration of the disturbed functions, they extirpated either the entire cerebral hemispheres (in reptiles and birds), or only the motor zones of the cerebral cortex (in mammals). For example, Bickel (1903) and Merzbacher (1901) removed the forebrain in frogs the extremities of which had previously been deafferentated. A similar combination of operations was performed by Trendelenburg (1906) on pigeons. Bickel removed the motor zones of the cerebral cortex in dogs after preliminary deafferentation of their paws and subsequent restoration of the disturbed functions. Ewald (1896) extirpated the cerebral hemispheres in pigeons and the motor zones of the cerebral cortex in dogs after preliminary destruction of their labyrinths. Luciani (1893) removed the motor zones of the cerebral hemispheres in dogs after extirpation of the cerebellum and subsequent recovery of the functions of standing and walking. Comparatively recently similar experiments, consisting of an analogous combination of operations, were performed by other investigators with the same purpose. Bethe, for example, removed the epipharyngeal ganglia in anthropoda and the motor zones of the cerebral cortex in dogs after preliminary amputation of some of their extremities. Anokhin removed the same zones in dogs after a preliminary cross-suturing of various nerves. Mettler (1944) did the same in monkeys after preliminary hemisections of the spinal cord. Undoubtedly these investigations played a positive role in the solution of the question which we are considering here, although they yielded heterogeneous and sometimes even contradictory results. This was explained by the limited number of experimental animals subjected to each kind of surgical operation, by the fact that each investigator studied the results of only one definite kind of surgical injury, and sometimes by the unsystematic and incomplete character of the experiments. From the experimental results of these investigations it was apparent that in invertebrates and lower vertebrates the higher parts of the central nervous system do not play any appreciable role in the compensation of the disturbed functions; in birds, however, these parts of the central nervous system play a definite (though not decisive) role in such compensation. As to the role of the motor zones of the cerebral cortex of dogs in the compensation of functions disturbed as a result of surgical injury to some other organs, the corresponding experimental data obtained by scientists are of a less definite and even of a contradictory character. Thus, according to the experiments of Luciani, Bickel, Mettler and Ewald, after the extirpation of the motor zones in dogs, the phenomenon of compensation which was previously observed disappears and then, after a considerable time, recovers to a certain degree. According to the experiments of Bethe and Anokhin, the removal of the sensory motor zones in previously operated dogs causes insignificant and transitory changes in the picture of the compensation which takes place after the original surgical injuries to the paws or nerves.

Apart, however, from the presence or absence of these contradictions, there was a definite defect which was common to all these experiments: the investigator removed only a small part of the cerebral cortex in the experimental animal. The results of such experiments could not provide a reliable scientific basis for the formation of a complete and correct idea of the role of the cortex as a whole in the compensation of the functions of a highly developed organism after injury to its other organs and systems. Contrary to the expectations of Bethe, this defect in experimentation on higher animals could not be adequately compensated for by data on the removal of the cerebral hemispheres in lower vertebrates and of the epipharyngeal ganglia in anthropoda, nor by the superficial observations of clinicians which, moreover, led to contradictory conclusions concerning the role of the cerebral cortex and the importance of learning in the phenomena of compensation. In order to solve this problem satisfactorily by means of experimentation, it was necessary to apply the method of complete removal of the cerebral cortex in experimental animals high in the evolutionary scale.

Our experimental work on the problem of compensation, conducted with our collaborators over the course of many years, was largely devoted to such a solution of this difficult and complex question, which is of both theoretical and practical importance.

Aiming at an overall study of this problem, we investigated the phenomena of compensation of functions after a series of surgical injuries of the organs and systems of the body which in most cases lead to profound and prolonged disturbances of the motor, vegetative and receptor functions. Specifically, we investigated the phenomena of compensation which occur after the amputation of extremities (Asratian), transplantation of the tendons of separate muscles of the extremities (Shamarina, 1956), deafferentation of the cervical muscles and extremities (Stefantsov, 1941; Drozdova, 1957; and Asratian), destruction of the labyrinths (Asratian), Brown-Séguard section of the spinal cord (Karamian, 1940; Dmitriev, 1951; Ivanova, 1953; Mirzoian and Oganesian, 1955; Askerov, 1956; Maksimova, 1958; Tkachenko, 1958; Adamian, 1956; Asratian), section of the dorsal or ventral half of the spinal cord at different levels (Barsegian, 1940; Shoshenko, 1955; Matinian, 1956; and Asratian), partial longitudinal splitting of the spinal cord in the zone of its various segments (Barsegian, Stefantsov, Ivanova), section of the lateral half of the brain stem at the level of the *corpora quadrigemina* (Nezlina, 1957), destruction of separate diencephalic and subcortical nervous formations (Stefantsov; Romanovskaia, 1957), extirpation of the cerebellum or destruction of its nuclei (Goncharova, Asratian), extirpation of the sympathetic ganglia (Stefantsov). At present we are also engaged in the investigation of the immediate and remote results caused by the transection of the lateral half of the medulla oblongata and by the focal destruction of its separate parts. The diagrams of these operations are shown in Figs. 1, 2, 3 and 4.

Our experiments were performed on lower vertebrates, birds and rabbits, but mostly on dogs. As a rule, each variant of the surgical injury of certain organs and systems was applied to a large number, often dozens, of experimental animals. The completeness of the removal of the cortex in mammals and of the forebrain in other animals, as well as the precision of the surgical injury, was in many cases verified by subsequent histological examinations.

Most of our experiments were carried out in the following manner: first a certain surgical injury was inflicted on the experimental animal; then the picture of the disturbance of functions immediately

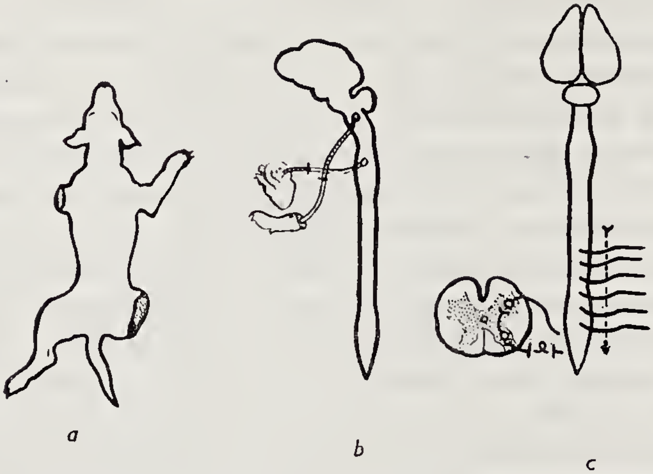

FIG. 1. Diagram illustrating the operations of: (a) amputation of extremities; (b) cross-anastamosis of the vagus and median nerves; (c) deafferentation of a hind extremity.

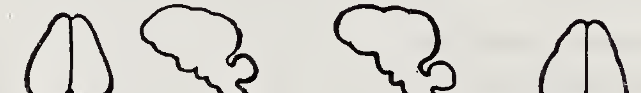

FIG. 2. Diagram illustrating the operations of: (a) lateral hemisection of the spinal cord; (b) dorsal hemisection of the spinal cord; (c) ventral hemisection of the spinal cord; (d) longitudinal section of the spinal cord.

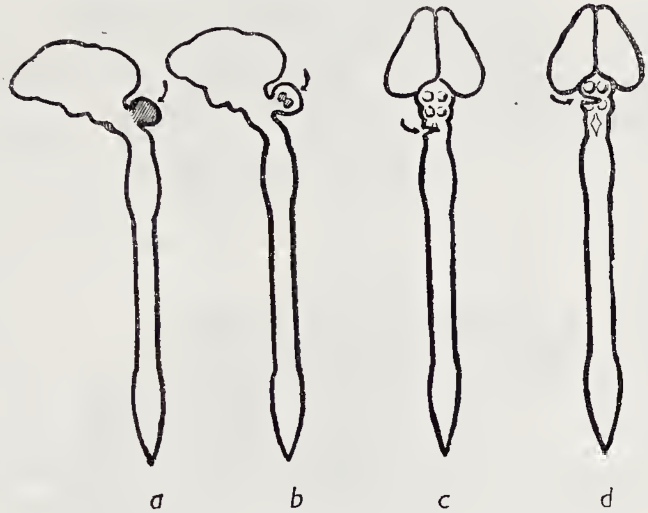

FIG. 3. Diagram illustrating the operations of: (a) total extirpation of the cerebellum; (b) destruction of the cerebellar nuclei; (c) lateral hemisection of the medulla oblongata; (d) lateral hemisection of the brain stem in the region of the *corpora quadrigemina*.

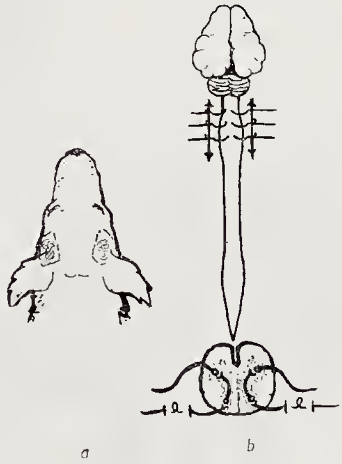

FIG. 4. Diagram illustrating the operations of: (a) destruction of the labyrinths; (b) transection of the dorsal roots of the three superior cervical nerves.

after the operation and the dynamics of the subsequent development of compensatory phenomena were thoroughly studied by means of various experimental methods. After the attainment of maximum compensation and of a relatively stable condition, we removed the cerebral hemispheres (in birds and lower vertebrates) or the cerebral cortex (in mammals) in the course of one operation or of two successive operations. A considerably smaller number of experiments were carried out in the reverse order: first the cerebral hemispheres or their cortices were removed in the experimental animals; after that, when the animals had recovered and could stand and walk, their extremities, receptors, spinal cord, etc. were further injured by surgical means.

We obtained the most abundant, varied and exact results from experimentation on adult dogs. These results are perhaps of particular importance from the practical point of view, and we shall therefore begin with a concise description of precisely these data and shall summarize these under the following four main categories.

1. The first category describes the dynamics of the restoration of the lost and disturbed functions in an organism which has been surgically injured. In adult dogs this process of restoration is chiefly in the nature of persistent, systematic and often slowly progressing training, of gradual and regular practice, perfection and consolidation of new motor habits, of new combinations of previous forms of movement (experiments of Barsegian, Ivanova, Urgandzhian, Nezlina, Maksimova, Goncharova, Shamarina, Tkachenko and Asratian). Figures 5, 6, 7, and 8 show this graphically; they present separate stages of restoration of the functions of walking and standing in dogs after a lateral hemisection of the spinal cord, its ventral hemisection, amputation of the extremities, and lateral hemisection of the brain stem. This was supported not only by systematic observations on the experimental animals, but also by data which we obtained in the course of studying this process by means of different methods of physiological experimentation: nerve chronaxies, muscle tone, recording of separate reflex reactions, examination of the supporting and locomotor functions of individual extremities, of the trajectory of walking, etc. Taken as a whole, these data accord fully with observations which have been carried out by clinicians for many years on persons suffering from certain types of mutilation. They also accord with data obtained in the past by a number of experimenters who investigated the consequences of those forms of surgical injury of the organism which we use in our experiments. On the other hand, our data fundamentally contradict the assertion of Bethe and others that the process of restoration of the disturbed

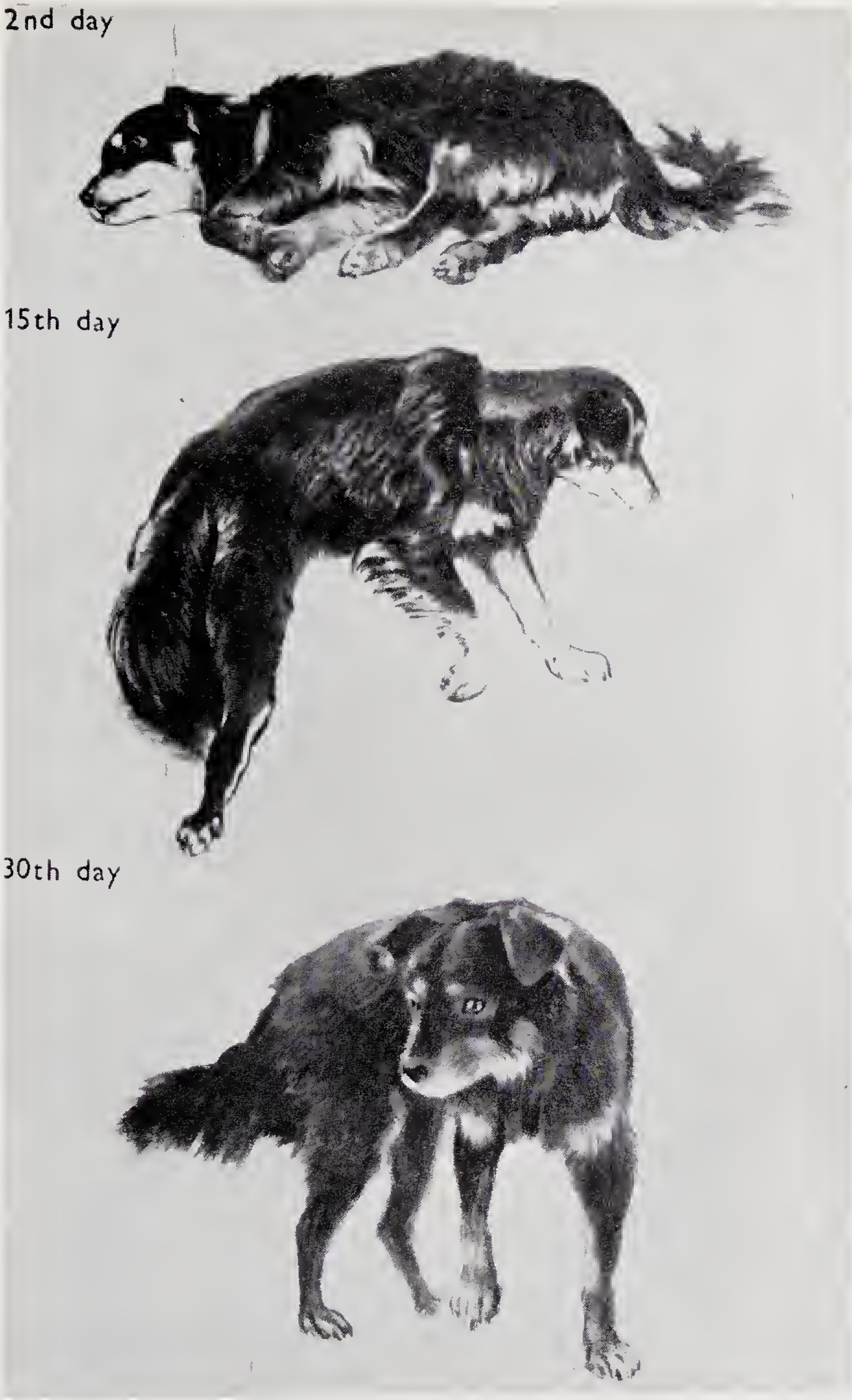

FIG. 5. Restoration of the functions of standing and walking in dog "Tserber" after a lateral hemisection of the spinal cord at the level of the superior cervical segments.

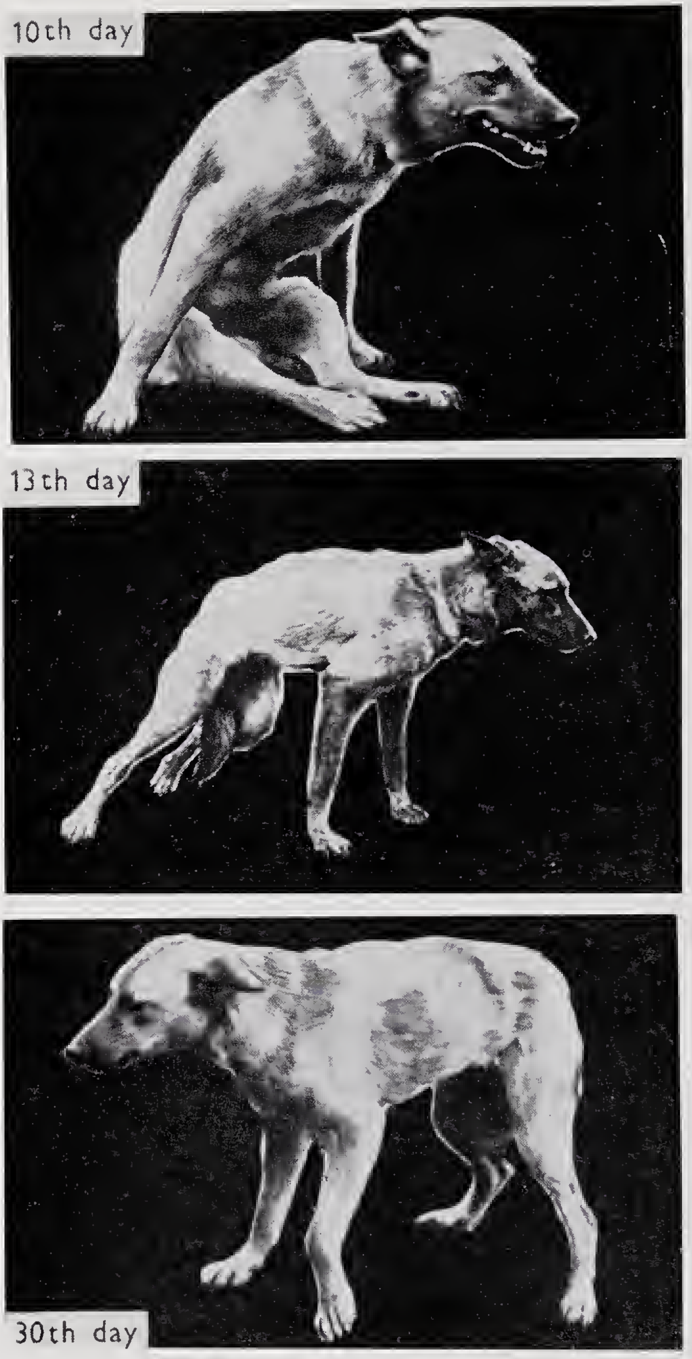

FIG. 6. Restoration of the functions of standing and walking in dog "Aslanka" after a ventral hemisection of the spinal cord at the level of the last thoracic segments.

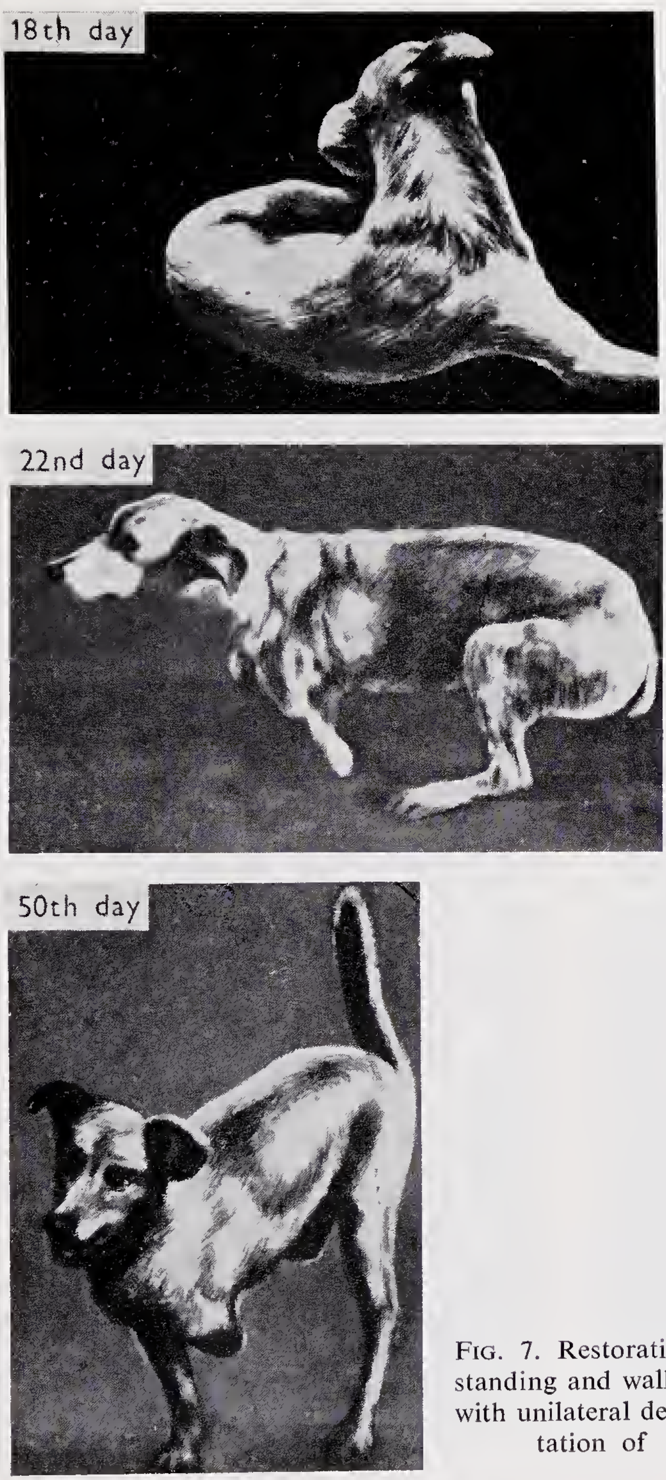

Fig. 7. Restoration of the functions of standing and walking in dog "Malchik" with unilateral decortication after amputation of two extremities.

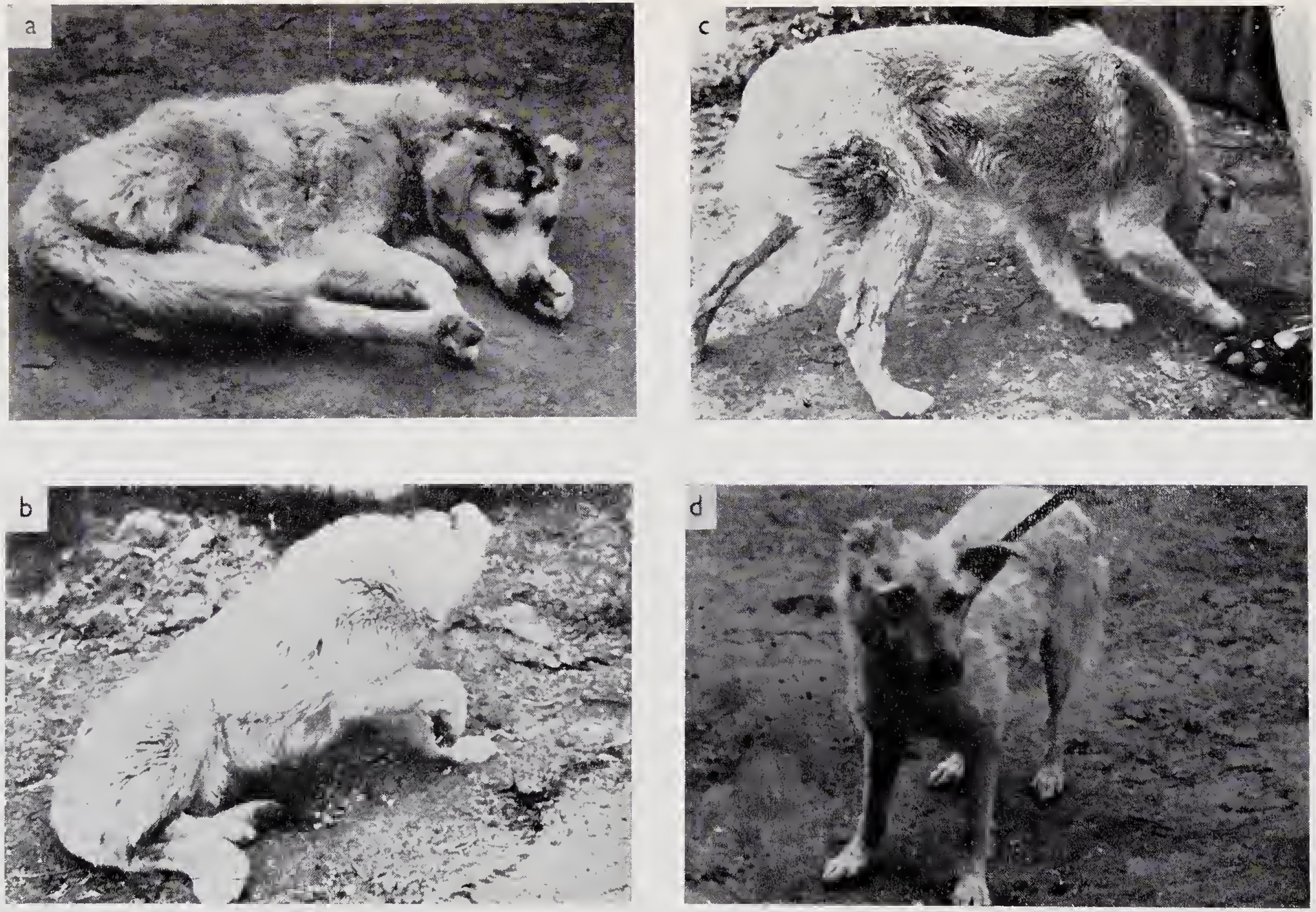

FIG. 8. Restoration of the functions of standing and walking in dog "Umnitsa" after a lateral hemisection of the brain stem in the region of the corpora quadrigemina: (a) 5 days after, (b) 9 days after, (c) 14 days after, (d) 60 days after the operation.

functions of an injured organism has the characteristics of an automatic, instantaneous reaction.

It must be pointed out that, according to our data, the rate and degree of perfection of the restoration of disturbed functions in these animals decrease considerably when their freedom of movement is limited and, on the other hand, substantially increase when this is extended, i.e. when the conditions for their training and learning are improved. Not long ago Grigorian (1957) demonstrated on a number of dogs in which two limbs had been amputated, that by means of intensive training it is possible substantially to accelerate the restoration of the functions of walking and standing in the two intact limbs.

We have further demonstrated that in dogs with an intact cerebral cortex the exclusion of vision, and particularly the destruction of the labyrinths, greatly retard the development of compensation after the amputation of two paws or after the transection of the posterior roots of three superior cervical nerves, but do not exert any marked influence on the course of compensation after lateral hemisection of the spinal cord and some other forms of injury.

Of definite interest also are our data showing that moderate doses of non-toxic soporifics, which intensify and prolong the daily sleep of the experimental animals during the immediate postoperative period, contribute to the rapid normalization of the condition of the central nervous system and subsequently increase the rate and quality of compensatory functions. Of a diametrically opposite chard acter is the influence of those factors which lead to deterioration- of the condition of the organism and to weakening of the nervous system; these include infectious and other diseases, poor conditions of maintenance, malnutrition, etc. These factors not only retard the restoration of the disturbed functions, but often cause a decompensation of functions and lower the level of compensation obtained earlier.

2. The second category of our general description of the results of our experimental work relates to data which demonstrate in an even more definite way the participation of the higher parts of the central nervous system in the development of compensatory adaptations. In cases where, depending on the kind of surgical operation, there occur chiefly local disturbances of functions of separate extremities in experimental dogs (for example, after lateral, ventral or

dorsal hemisections of the spinal cord or lateral hemisection of the midbrain), the electrodefense, auditory, visual and tactile conditioned reflexes of the affected extremities, which were elaborated prior to the operation, become disturbed and recover simultaneously

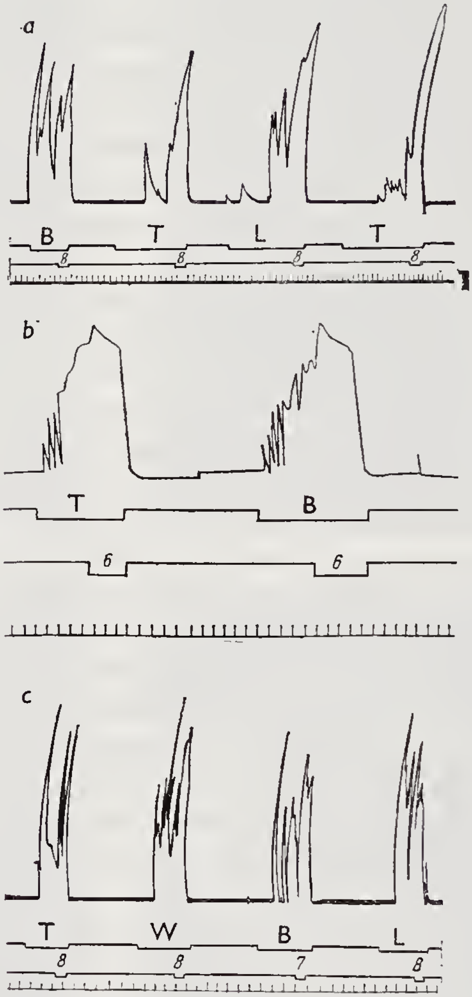

FIG. 9. Kymograms of the electrodefense motor conditioned reflexes of the hind extremities in dogs after (a) lateral, (b) ventral and (c) dorsal hemisections of the spinal cord at the level of the last thoracic segments. B = bell, T = tactile, L = light, W = whistle.

with the disturbance and recovery of their supporting and locomotor functions, and often even somewhat earlier (according to the data obtained by Novikova and Bokova, Urgandzhian, Ivanova, Nezlina and Asratian. Figure 9). It is also possible, however, to elaborate new visual, auditory and tactile electrodefense conditioned reflexes of the affected extremities. Conditioned reflexes often emerge even during the early stages of restoration of functions, although at that time they do not exhibit any particular stability.

The following observations also indicate the existence of a connection and interaction between the cerebral cortex and the affected half of the spinal cord. In a number of experiments performed in our laboratory Maksimova demonstrated that a lateral hemisection of the spinal cord at the level of the inferior thoracic and especially the superior cervical segments, in some of the experimental animals considerably suppresses the electric activity of the cortex of the contralateral cerebral hemisphere. This leads to a pronounced asymmetry in the intensity of the electric activity of the contralateral points of the hemispheres immediately after the operation. We shall not consider here the essence of the suppression which is evoked by the trauma of the spinal cord; we shall only point out that this is a temporary phenomenon. With the stabilization of the reflex activity of the affected extremities and with the development of the compensation of the disturbed motor and sensory functions, it becomes possible not only to intensify the electric activity of the cortex of this hemisphere by stimulating the affected extremities, or by their natural movement, but also to re-establish the level of its background electric activity and to bring it into conformity with the degree of activity of the other cerebral hemisphere (Fig. 10). A very interesting phenomenon is invariably observed during the experiments: the electric activity of the cortex of the affected hemisphere not only reaches the level of intensity of that of the intact hemisphere, but for some time even surpasses it.

3. Our third category concerns the influence of extirpation of the cerebral cortex on the compensatory phenomena which arise after preliminary surgical injury of different organs and systems. In adult dogs the removal of the cortex of one hemisphere leads to the disappearance of the compensatory adaptations which develop after the preliminary operation, but this disappearance is of a temporary character. Later, a second restoration of the disturbed functions takes place and, as a rule, it is as gradual and slow as that after the preliminary operation. The removal of the entire cerebral cortex leads to an almost complete and irreversible disappearance of these

compensatory adaptations (according to the data obtained by Ivanova, Urgandzhian, Goncharova, Nezlina and Asratian). When we surgically injure the spinal cord, extremities or receptors of adult dogs in which the entire cerebral cortex has long previously been removed, the functions which were disturbed and lost as a result of these operations never recover (Asratian). Some illustrative examples are given in corresponding figures, showing that as a result of complete cerebral decortication in adult dogs there occurs an irreversible disappearance of compensatory phenomena which develop after the amputation of two extremities (Fig. 11), lateral hemisection of the spinal cord at the level of the last thoracic segments (Fig. 12) and of the superior cervical segments (Fig. 13), cross anastomosis of the median and vagus nerves (Fig. 14), ventral hemisection of the spinal cord at the level of the middle thoracic segments (Fig. 15), dorsal hemisection of the spinal cord at the level of the middle thoracic segments (Fig. 16b), deafferentation of the hind leg (Fig. 16a), and extirpation of the cerebellum (Fig. 17).

We obtained all these data on nearly 100 adult dogs in which we surgically injured certain peripheral or central organs or nerve conductors, and in addition removed the entire cerebral cortex; these experimental dogs lived in the resultant conditions for many months, and in some cases even for a number of years. Macro- and micromorphological investigations of preparations of the brain of many operated dogs, carried out in the laboratories of L. Pines, V. Doynikov, M. Aleksandrovskaia and F. Brazovskaia, have shown that as a rule we perform a complete cerebral decortication.

A general survey of these preparations is given in Figs. 18, 19 and 20. This gives us sufficient reason to believe that the reliability of the above data is beyond any doubt.

Some details of our experiments are of great importance for a fuller comprehension and proper evaluation of the role of the cerebral cortex in the development of compensatory adaptations in adult animals. As is to be expected, the removal of only one hemisphere may cause reactions of various degrees of intensity and duration depending upon whether the decorticated hemisphere is on the same or opposite side as that of the initial surgical injury to the extremities, spinal cord, nerves, etc. (Fig. 21). For example, if both left paws of the experimental dog have been amputated and the dog has learned to stand and move by using its right paws, then after subsequent

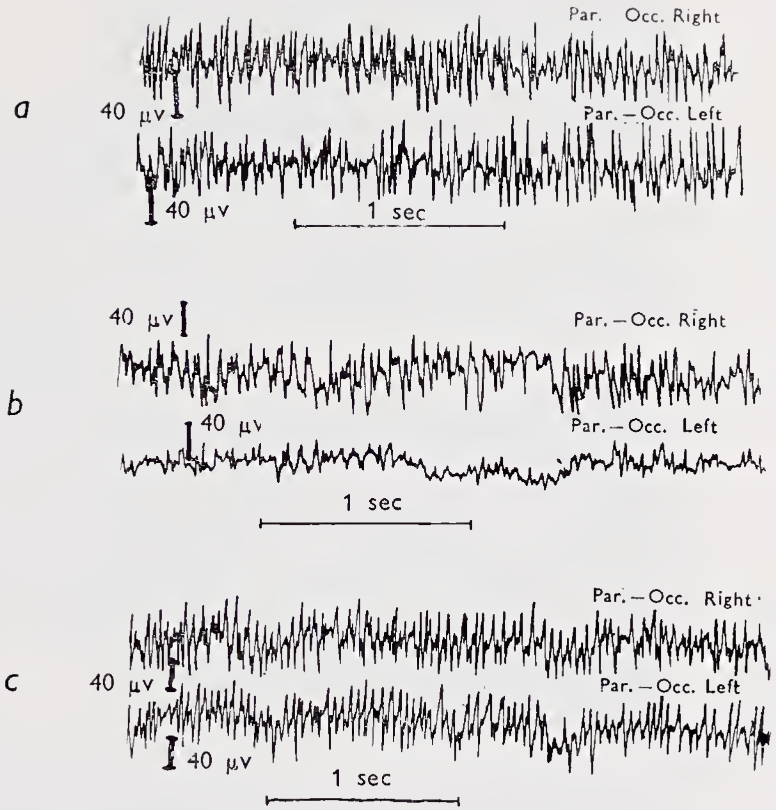

FIG. 10. Electroencephalogram of the right and left cerebral hemispheres in dog "Alma": (a) normal, (b) 3 days after a right lateral hemisection of the spinal cord at the level of C_2, (c) 40 days after the operation.

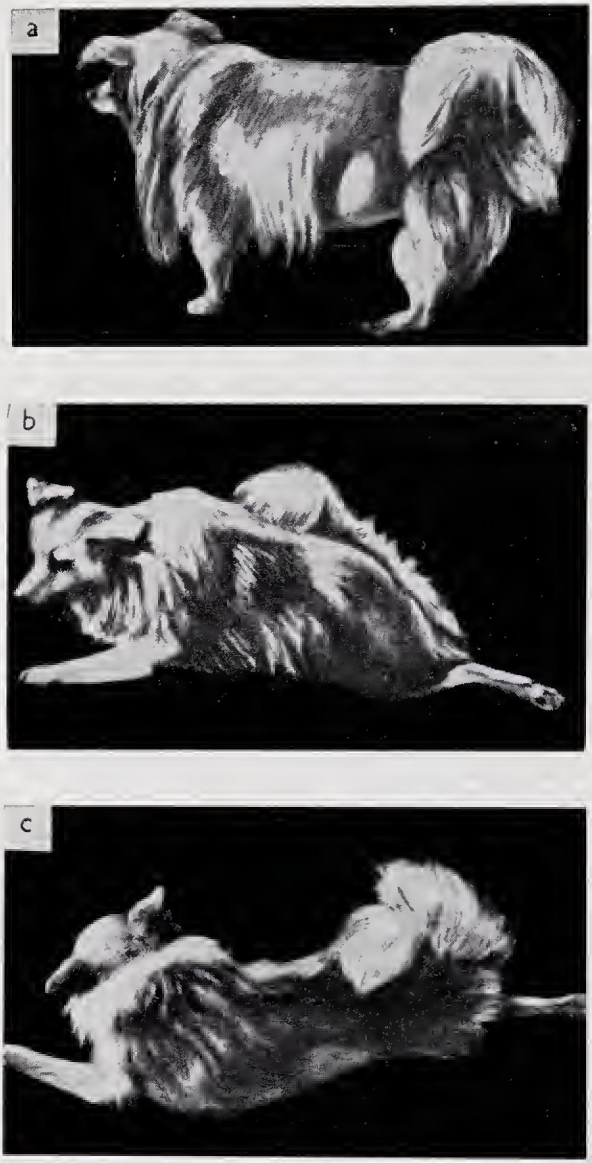

FIG. 11. Influence of decortication of the brain on the functions of standing and walking in dog "Krasavitsa" with two amputated extremities: (a) after decortication of one hemisphere, (b) and (c) 3 months after decortication of the second hemisphere.

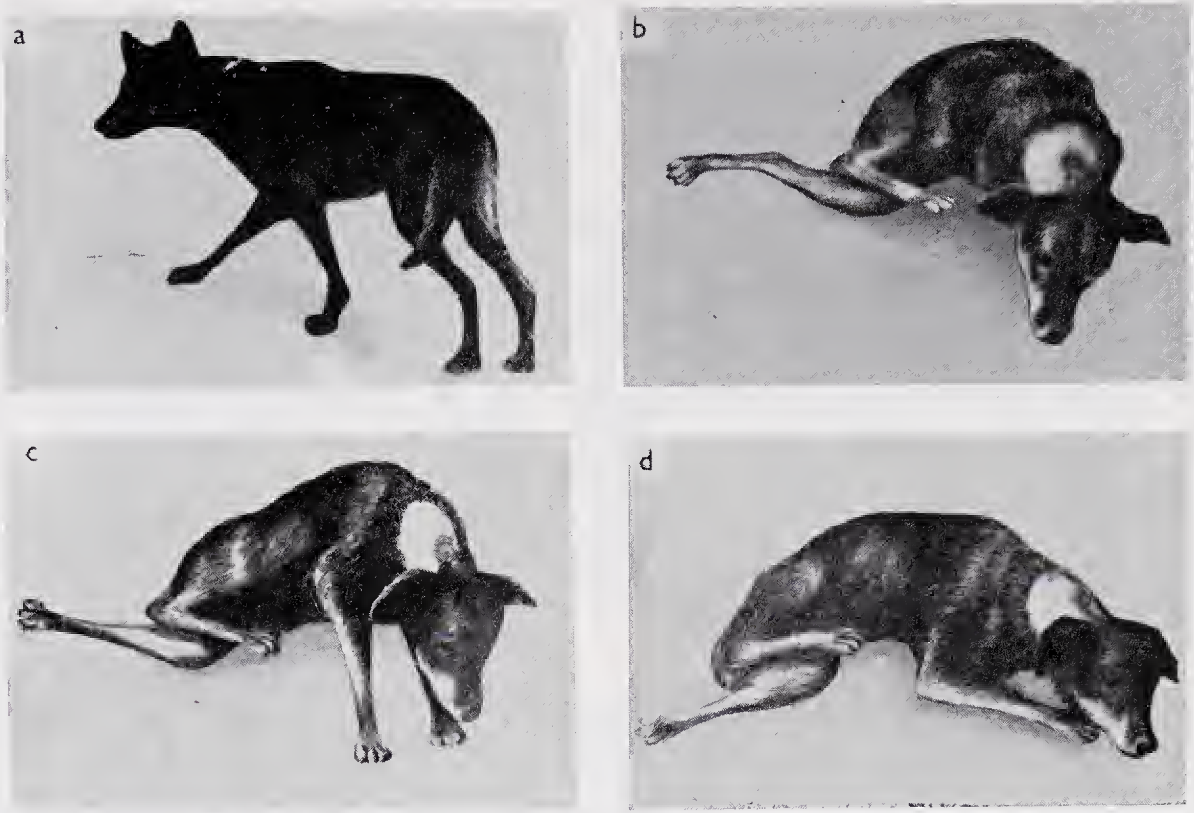

FIG. 12. Influence of cerebral decortication on the supporting and locomotor functions of the hind extremities in dog "Addis" after a lateral hemisection of the spinal cord at the level of the last thoracic segments: (a) one month after hemisection, (b), (c) and (d) after complete cerebral decortication.

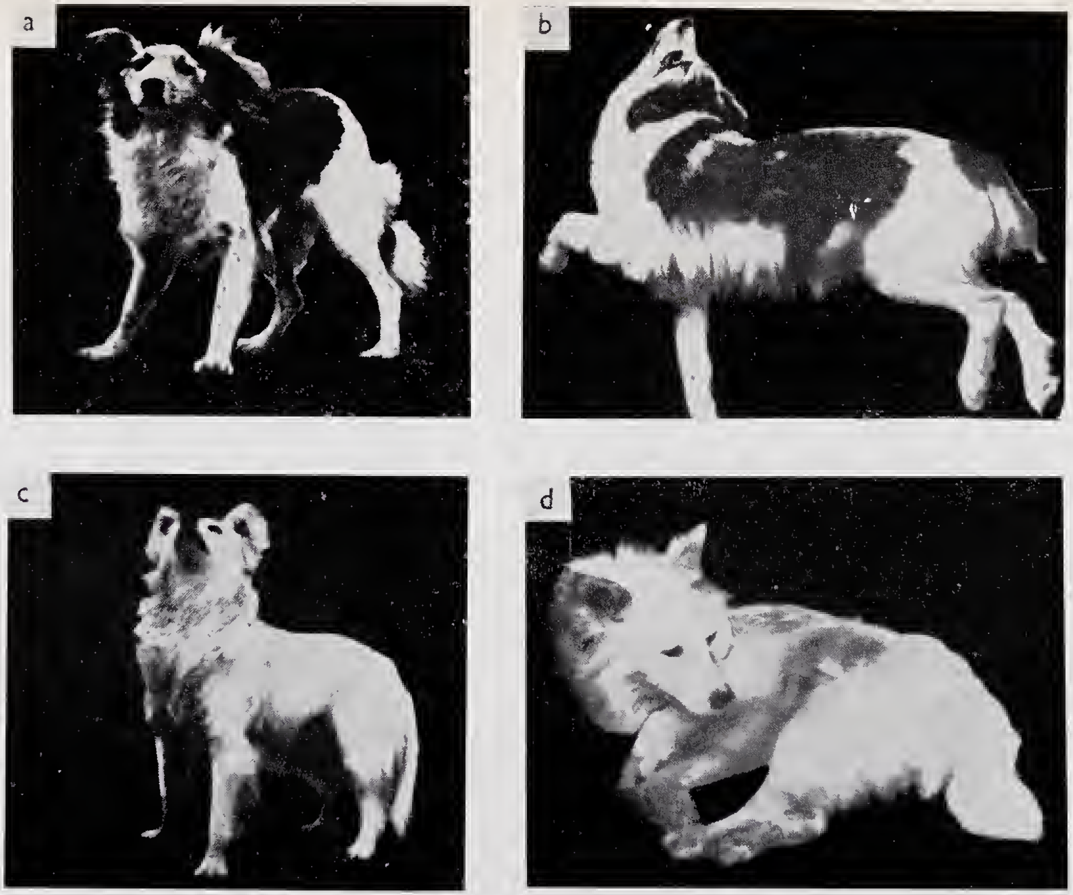

Fig. 13. Influence of cerebral decortication on the functions of standing and walking in dogs "Elma" and "Sharik" after lateral hemisection of the spinal cord at the level of the superior cervical segments: (a) "Elma" 6 months after unilateral decortication, (b) 2 months after bilateral cerebral decortication, (c) "Sharik" 6 months after unilateral decortication, (d) 9 months after bilateral cerebral decortication.

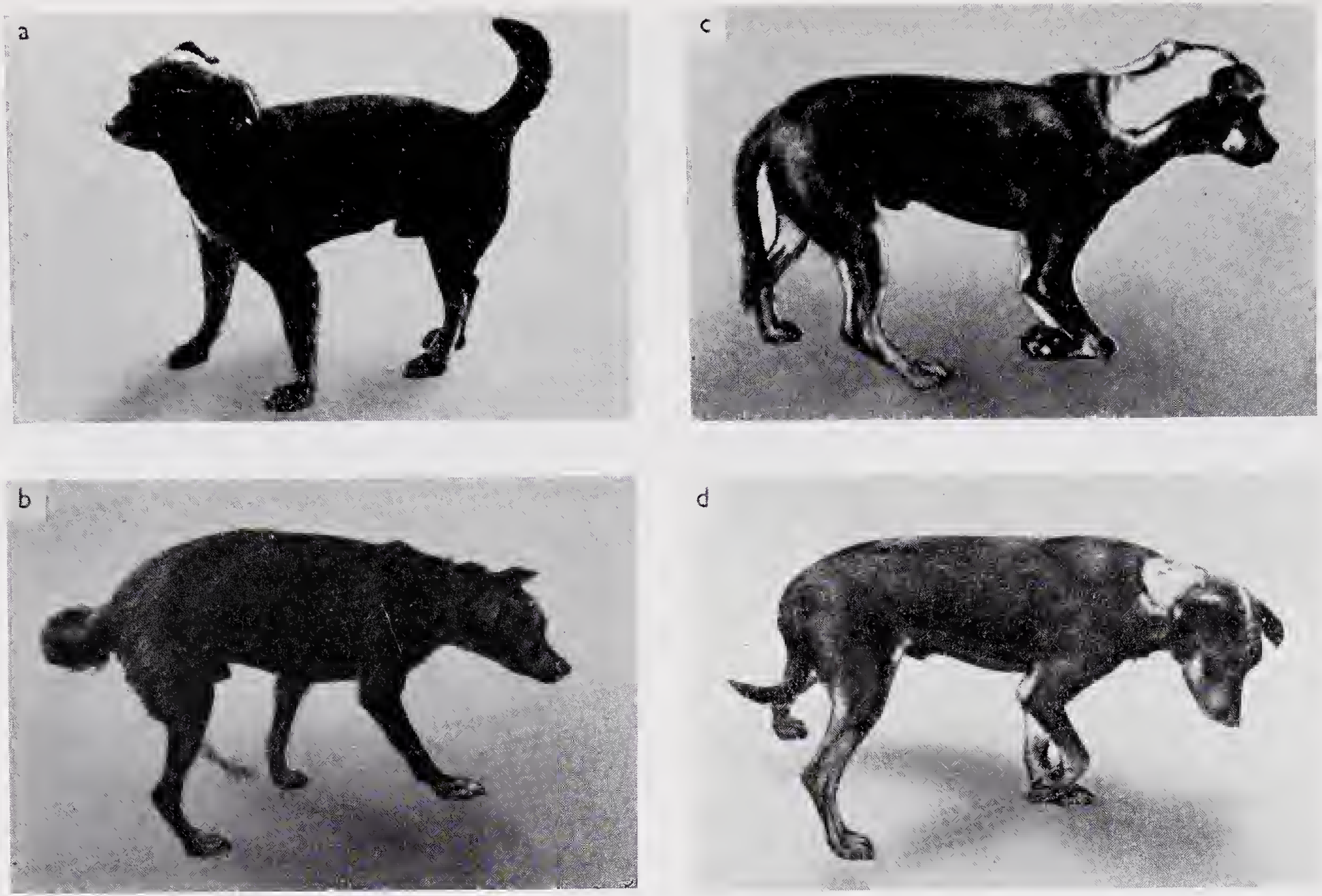

FIG. 14. Influence of cerebral decortication in dogs "Radius" and "Takhits" on the supporting and locomotor functions of the right fore extremity with cross-anastomosis of the vagus and median nerves: (a) "Radius" before cerebral decortication, (b) after cerebral decortication, (c) "Takhits" before cerebral decortication, (d) after cerebral decortication.

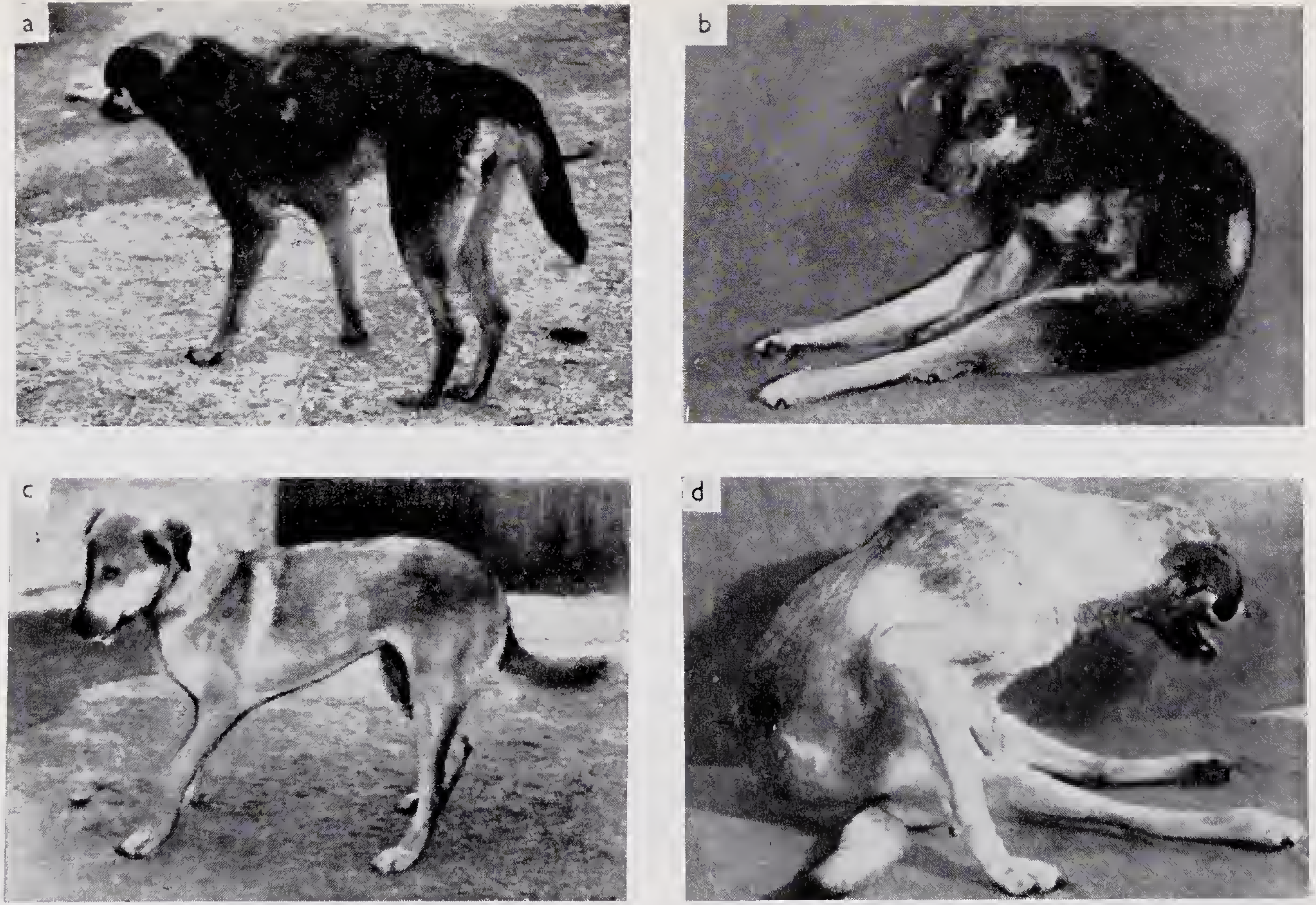

FIG. 15. Influence of cerebral decortication on the supporting and locomotor functions of the hind extremities in dogs after ventral hemisection of the spinal cord at the level of the middle thoracic segments: (a) dog "Umnitsa" 85 days after operation of the spinal cord, (b) the same dog 25 days after complete cerebral decortication, (c) dog "Damka" 85 days after spinal operation, (d) the same dog 6 months after complete cerebral decortication.

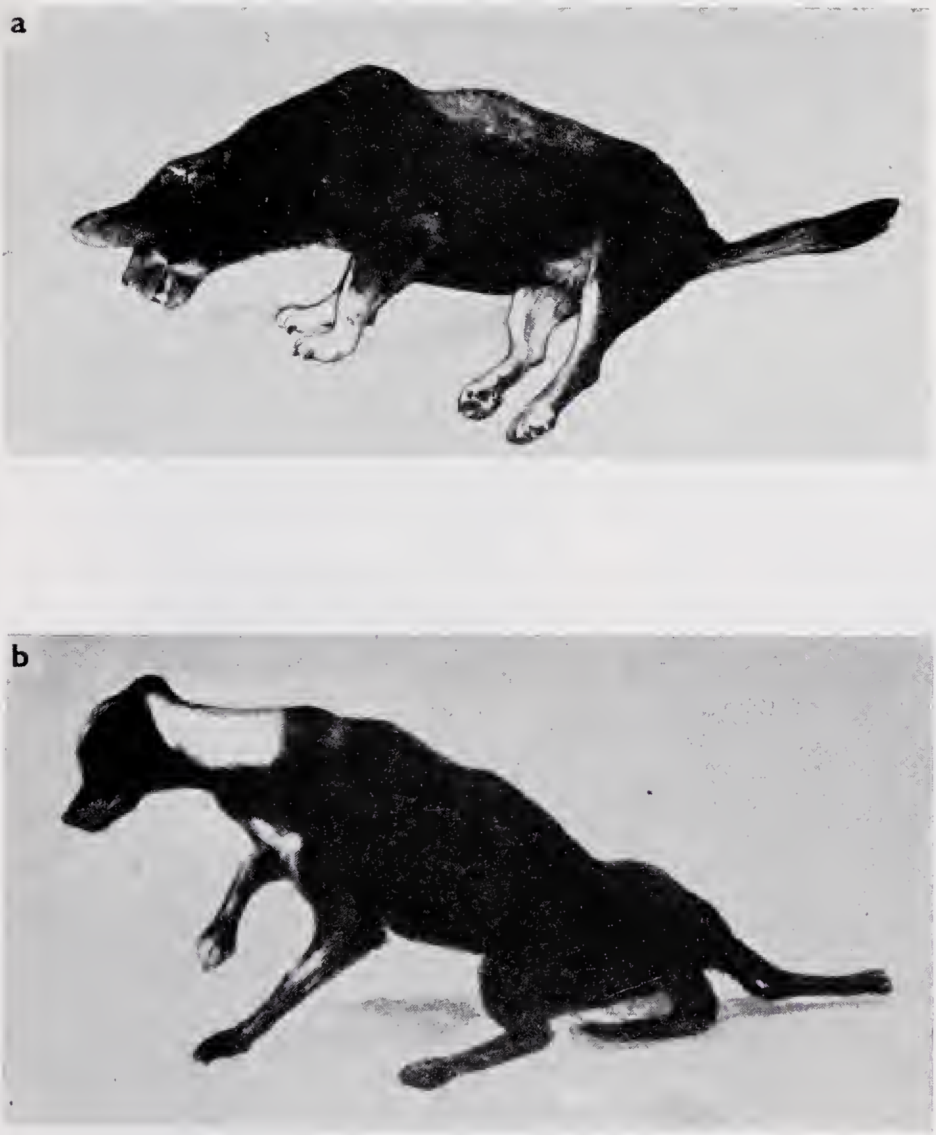

FIG. 16. Influence of cerebral decortication on the supporting and locomotor functions of the hind extremities: (a) in dog "Ryzhko" with a deafferentated left hind extremity, and (b) in dog "Tsygan" with dorsal hemisection of the spinal cord at the level of the inferior thoracic segments.

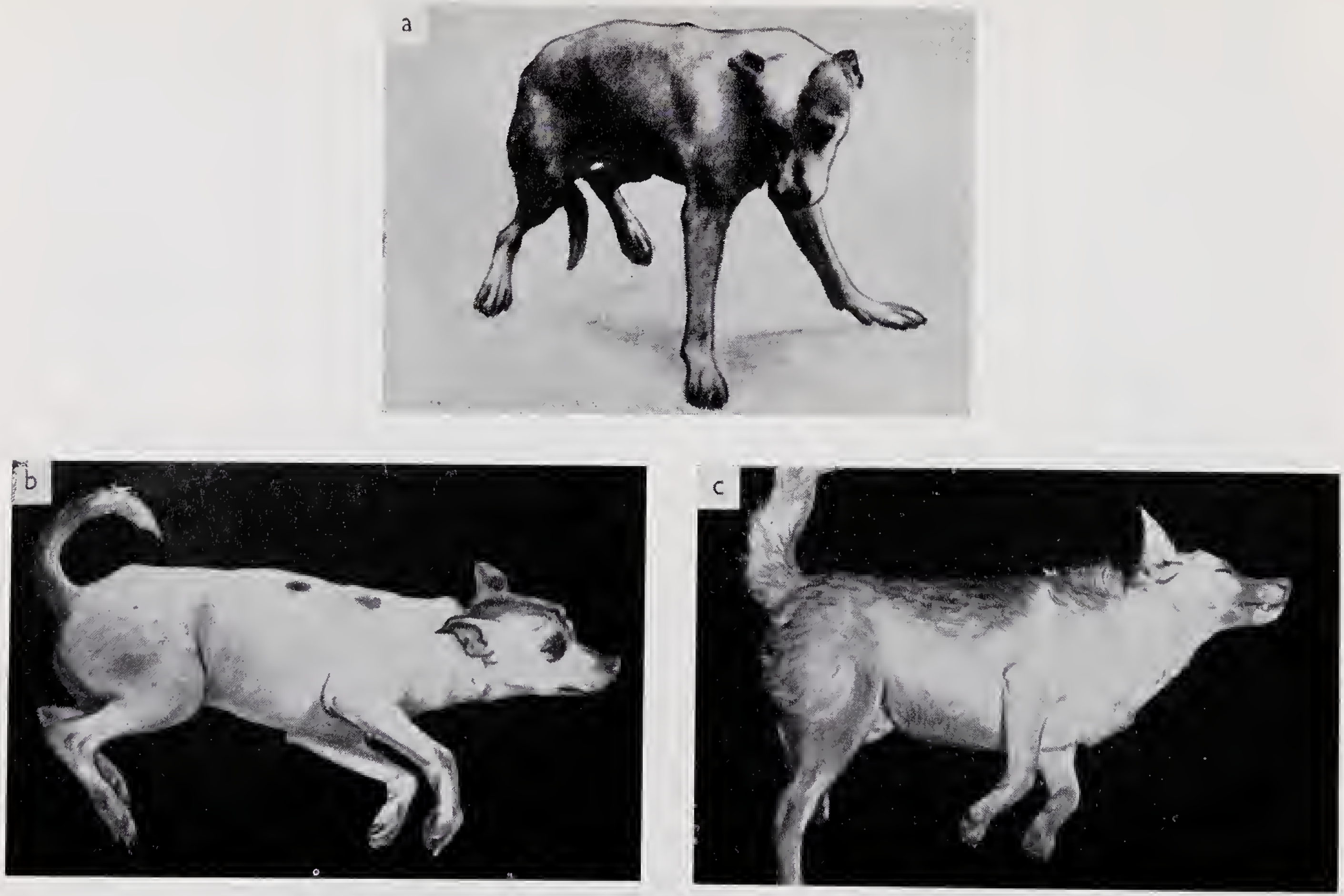

Fig. 17. Influence of cerebral decortication on the functions of standing and walking in decerebellated dogs "Lebed" and "Zliuka": (a) "Lebed" after unilateral decortication, (b) after the decortication of the second hemisphere, (c) "Zliuka" after complete cerebral decortication.

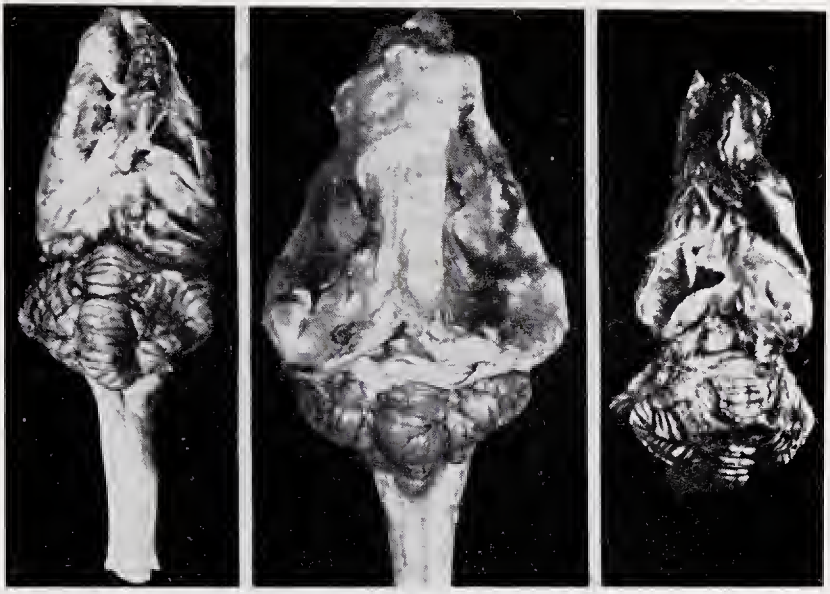

FIG. 18. Brain preparations of dogs after cerebral decortication.

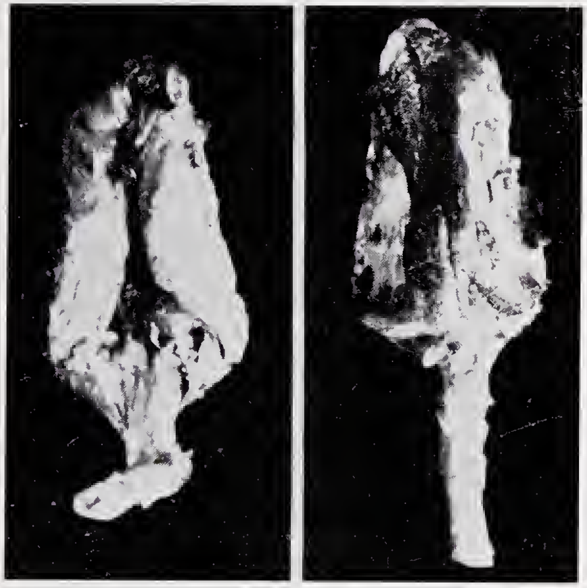

FIG. 19. Brain preparation of dog "Zliuka" after extirpation of the cerebellum and cerebral decortication.

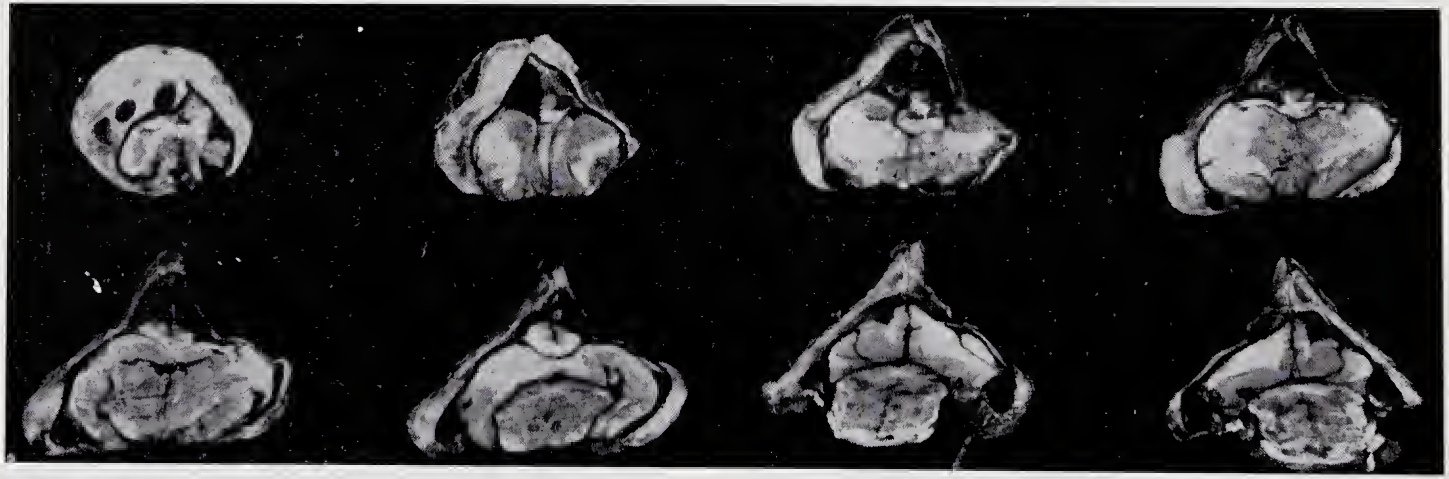

FIG. 20. Frontal sections of a preparation of the decorticated cerebrum of dog "Aguti".

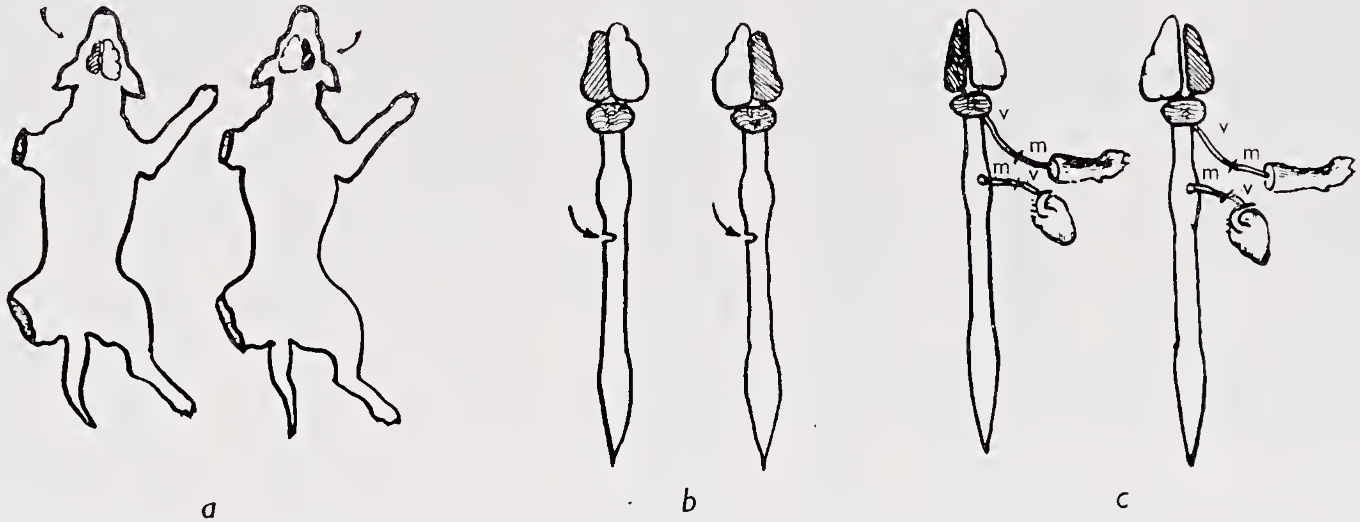

FIG. 21. Diagram illustrating the significance of the ipsilateral or contralateral decorticated cerebral hemisphere for laterally amputated extremities (a), to a lateral hemisection of the spinal cord (b), and (c) to a cross-anastomosis of the vagus and median nerves.

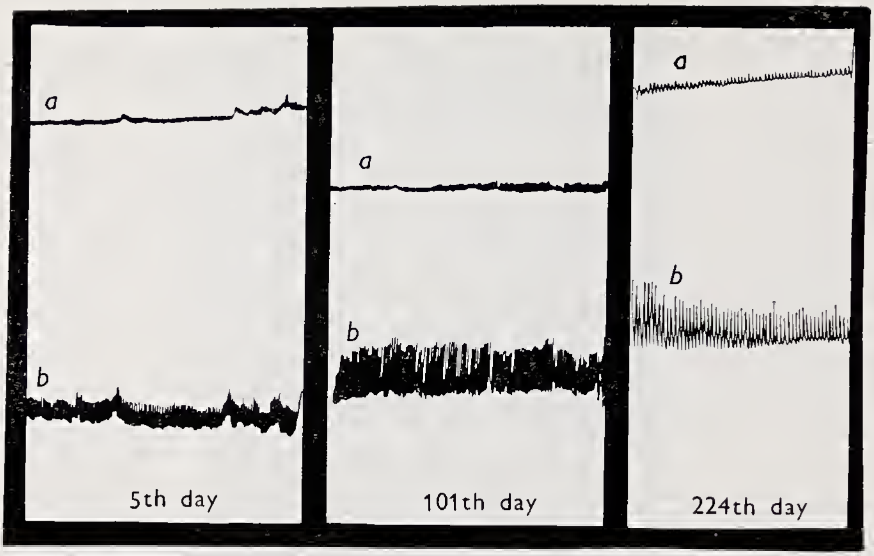

FIG. 22. Bilateral pneumogram in dogs after lateral hemisection of the spinal cord at the level of the superior cervical segments (5, 101 and 224 days after the operation): (a) ipsilateral hemisection, (b) contralateral hemisection.

decortication of the ipsilateral, i.e. left, hemisphere only, the functions of standing and moving become profoundly and protractedly disturbed (this lasts a year and over), while after decortication of only the contralateral hemisphere these functions are less profoundly disturbed and recover much sooner, within 20–25 days. For the sake of greater clarity, a combination of these operations is diagrammatically shown in Fig. 21. There is a similar difference between the results of extirpation of the cortex of one hemisphere or the other in dogs with a lateral hemisection of the spinal cord. The decortication of the hemisphere which is ipsilateral in relation to the spinal hemisection leads to a more profound and protracted disturbance of the restored functions than does the decortication of the contralateral hemisphere. The combinations of these operations also are diagrammatically shown in Fig. 21b. It is easy to see that both in the case of amputation of the paws and in the case of hemisection of the spinal cord, the difference between the results of decortication of the ipsilateral and of the contralateral hemispheres is determined by the fact that the cross intracentral pathways between the cerebral cortex and the spinal cord markedly predominate over the direct pathways. For the same reason, when the nerves of an extremity have been cross-sutured or when an extremity has been deafferentated, more severe effects occur after decortication of the contralateral hemisphere. The combination of these operations is diagrammatically presented in Fig. 21c.

The fundamental significance of all these findings consists in the fact that the effects of the removal of the cerebral cortex on previously restored functions cannot be interpreted as the result of a general traumatic and weakening action of this severe surgical operation *per se* on the general condition of the organism, but that a far more essential role in this respect is played by the special functional interrelations between the cortex and the previously injured central and peripheral organs.

This important conclusion is also supported by the following data. When the injury of the spinal cord or nerves evokes a predominantly local disturbance of the supporting or locomotor functions of certain extremities (which are later compensated), the removal of the cortex of both hemispheres eliminates the local compensatory phenomena without affecting to any appreciable degree the supporting and locomotor functions of the other extremities. If, for example, in a dog the lateral half of the spinal cord at the level of the last thoracic segments has initially been transected and the disturbed functions of the ipsilateral hind paw have already been restored, then, after complete decortication the functions of this paw again become disturbed; the same applies to some extent to the functions of the other hind paw, but the functions of the fore paws are not affected at all. Such a dog is able to raise itself on its fore paws and to move by their means, dragging the inactive hind paws behind (Figs. 12, 15 and 16c).

The same situation is observed after complete decortication in dogs in which there was a previous dorsal or ventral hemisection of the spinal cord at the level of the lower thoracic segments, or the nerves of a certain extremity were previously transected and cross-sutured, or the extremity was deafferentated. The restored functions of the surgically injured extremities suffer greatly and the compensation which had developed disappears, while changes in the functions of the other extremities are imperceptible (Fig. 14).

Some other results of our experimental work on this problem are of some interest. These data might at first appear to disagree with the above observations, but actually they are in full accord. For example, some adaptive phenomena develop in these animals rapidly and without the decisive participation of the cerebral cortex, i.e. they persist even after its removal. This occurs under two conditions: when the injury inflicted on the organism is not severe and evokes no profound disturbance, and when the disturbed functions are of a specific nature. The first condition includes, for example, the recovery of functions after the amputation of only one paw, after a minor injury of the spinal cord, after the cross-suturing of certain nerves which are of secondary importance in the functioning of the given organ, etc. The second condition includes a rapid readjustment of functions in the course of the so-called cross phenomenon of the phrenic nerve which occurs after hemisection of the spinal cord below the medulla oblongata and after subsequent transection of the opposite phrenic nerve. In our experiments this phenomenon appeared not only after the complete removal of the cerebral cortex, but also after the removal of the diencephalon and even of the mesencephalon, i.e. in bulbar animals.

On the other hand, not every disturbance of the functions of the organism can be satisfactorily compensated even when the cerebral cortex is intact. This occurs under two conditions: first, when the injury inflicted on the organism is very severe, for example, when considerably more than half the diameter of the spinal cord is transected, or when several segments of the spinal cord are split sagitally in those of its parts which directly innervate the fore and hind extremities; second, when the disturbed functions do not markedly depend on cortical regulation. For example, transverse transection of a lateral half of the spinal cord at the level of the first cervical segments leads to a profound disturbance of the supporting and locomotor functions of the homolateral extremities, as well as of the function of the homolateral respiratory muscles. Although the functions of the extremities are fully restored after a period of 30–40 days, the function of the respiratory muscles does not recover to any appreciable degree for many months or even a year and longer (data obtained by Ivanova and Asratian. Figure 22). The above observations agree with some of our preliminary data which show that the role of the cerebral cortex in the restoration of the vegetative functions in adult higher animals, disturbed as a result of our operations, is much less important than in the restoration of the somatic functions (Stefantsov.)

In recent years we have accumulated some experimental data concerning the disturbance and restoration of the functions of the organism after various surgical lesions of the medulla oblongata. It is self-evident that in order to study the results of lesions of the medulla oblongata under chronic conditions, it was necessary to keep alive the animals that had been subjected to surgical operations. This problem, as is well known, is extremely complicated and has until recently been considered practically insoluble. We succeeded in developing a regimen which permitted the preservation for several months of the lives of most of the young dogs, and especially the puppies, after various surgical lesions of the medulla oblongata. I cannot here describe in detail the immediate consequences of various lesions of the medulla oblongata which are in themselves of great interest, but shall only note them from the standpoint of the problem of compensation of functions.

Jointly with our co-workers Drozdova, Goncharova and Stefantsov we investigated the disturbances and restoration of some somatic and vegetative functions in dogs and puppies after the destruction of the dorsal nucleus of n. vagi, as well as after lateral hemisection and longitudinal section of the medulla oblongata. As was to be expected, the above-mentioned lesions of the medulla oblongata evoked in all the experimental animals strongly pronounced changes in the function of the respiratory and cardiovascular systems. In the overwhelming majority of cases respiration stopped immediately after the operation and the level of the blood pressure changed, predominantly showing a sharp decrease. The application of artificial respiration for several hours and the administration of a number of medications made it possible to restore normal respiration and to raise the level of the blood pressure.

Along with these disorders, which proved common to all the animals that had been subjected to operations, there also took place some specific disturbances, depending on the character and localization of the lesion in the medulla oblongata. For example, in animals with a left hemisection of the medulla oblongata we observed unilateral respiration, namely in the side of the operation, while on the opposite side it was paralyzed. Only three months later bilateral respiration was restored and the frequency as well as the amplitude of the respiratory movements of both halves of the thorax became equal. Along with disturbances of the respiratory and cardiovascular systems, the operated animals manifested disorders of the supporting-locomotor functions, namely a loss of the capacity to stand and to walk, a lowering of the muscle tone and a disruption of the coordination of movements. Eventually these disturbances also become compensated. The intensity and duration of these disturbances and the degree of compensation depended also on the character and localization of the lesion in the medulla oblongata. Disturbances resulting from hemisection proved to be the most stable and the least susceptible to complete compensation. It should be pointed out that after a lateral hemisection of the medulla oblongata there developed in the animals a stable Bernard–Horner syndrome (sympathetic ophthalmoplegia) as well as paresis or paralysis of the left sublingual nerve.

In some dogs with lateral hemisection of the medulla oblongata we removed the cortex of one cerebral hemisphere when the disturbed functions reached the limit of possible compensation; in one of the dogs we also removed the cortex of the second hemisphere. In the case of this lesion of the central nervous system also, the extirpation of the cortex of one hemisphere resulted in a profound and protracted, but to some degree reversible, decompensation of functions, while a complete removal of the cortex led to an irreversible decompensation.

It should be noted that the significance of the age factor in the dynamics of the disturbance and restoration of functions in the case of a lesion of the central nervous system (noted by us and by some other scientists) appeared especially clearly in lesions of the medulla oblongata. Puppies are far more resistant to lesions than adult dogs, and the disturbance of functions is less profound and lasting in them than in the adults. Moreover, in case of severe lesions of the medulla oblongata (for example, in the case of hemisection) we succeeded in preserving for long periods of time only the lives of puppies and not of adults.

From the above it follows that *in adult higher animals the cerebral cortex as a rule plays a decisive role in the restoration of the postural, supporting and locomotor functions disturbed as a result of severe organic injury of the central and peripheral organs and nerves.* These are some of the basic findings obtained in connection with this investigation. We believe also that any deviations from the above-mentioned findings, namely, the data which concern the role of the cortex in the compensation of functions after a slight or a very severe injury of the organism, as well as in the compensation of functions which in general are not greatly dependent on cortical regulation, do not detract from, but rather underline, the significance of these findings.

4. The fourth category in our general description of the material obtained concerns the results of our investigations on the characteristics of the development of compensatory adaptations in animals which are at different phylogenetic and ontogenetic evolutionary levels and on the role of the higher parts of their central nervous systems in the process of compensation. These results differ greatly from those which were obtained on adult dogs. Essentially they are as follows: the lower the levels of phylogenetic and ontogenetic evolution of the animals, the less severe, as a rule, are the results caused by injury of different organs of the central nervous system and of some peripheral nerves, the more rapidly do the compensatory adaptations develop, and the less important is the participation of the higher parts of the brain in their achievement. For example, in puppies one to three months old, hemisection of the lateral, ventral or dorsal half of the spinal cord causes considerably less pronounced

disturbances of the supporting and locomotor functions of the extremities than in adult dogs and the disturbed functions are much more rapidly restored than in the latter, namely, in 5–10 days instead of 30–45. A complete deafferentation of one of the hind extremities in puppies two to four months old leads to profound disturbances in the supporting and locomotor functions of this extremity. It is true that the restoration of the disturbed functions is in this case much slower (1·5–2·5 months) than after the hemisection of the spinal cord in puppies of the same age; nevertheless, this is approximately half of the time required for the restoration of functions in adult dogs after a similar deafferentation of their extremities.

In spite of this difference in the time required for restoration of the supporting and locomotor functions in puppies after these different types of injuries, the results of cerebral decortication are almost the same in both cases. The removal of the cortex of both hemispheres in considerably older puppies does not result in the permanent disappearance of the already developed compensatory adaptations, as is the case in adult dogs, but only in their temporary disappearance for a certain period immediately after the operation. With the lapse of time the disturbed postural, supporting and locomotor functions in the decorticated puppies recover, although this recovery is far from being as complete as it was before the removal of the cortex (according to the data of Barsegian, Ivanova, Drozdova, Isaakian, Dimitriev, Urgandzhan and Asratian). The more rapid and complete recovery of the disturbed functions in puppies undoubtedly indicates the high plasticity of their central nervous systems which are still immature and morphologically and functionally underdeveloped. As to the profound but transitory effect of cerebral decortication on the restored functions in such puppies, this is by no means an indication of the limited capability of the cortex; rather, it shows that at this age the specific role of the subcortical nervous formations in the integrative activity of the nervous system is considerably greater than in adult animals.

These two peculiarities of the central nervous system in young puppies are also demonstrated by the following data obtained in our laboratory: puppies of this age, in contradistinction to adult dogs, are capable of restoring the disturbed supporting and locomotor functions of their extremities after a sagittal splitting of the spinal cord in the zone of the segments which innervate these extremities. In this case, however, the functions are very profoundly disturbed, recover very slowly (after 1 or 1·5 months), and do not reach any appreciable degree of perfection. It is also characteristic that cerebral decortication in these experiments leads not to a temporary disappearance of the compensation attained, as happens after hemisections of the spinal cord in young puppies, but to its permanent and irreversible disappearance (experiments of Ivanova). Thus, although in older puppies the specific role of the subcortical formations in the activity of the higher parts of the central nervous system is greater than that in adult dogs, nevertheless their cerebral cortex plays a more important regulatory role than in younger puppies.

It must be pointed out that the literature contains a number of experimental data and clinical observations which show that surgical injury of the spinal cord and of different parts of the brain in puppies, kittens and young rabbits, as well as in children, evokes less profound protracted disturbances than in the respective adult animals and humans (Bekhterev, 1885; Soltman, 1876; Khokhlova, 1954; Babchin, 1954; Kennard, 1944; Baiandurov, 1949; and others). It is evident that the results of our systematic investigations to some degree corroborate this hypothesis and develop it further. As to our data concerning the role of the cerebral cortex in the restoration of functions that have been disturbed and lost as a result of other organic lesions of the growing organism, these are entirely original.

Up to the present time peculiarities due to age in the development of compensatory adaptations in higher animals after lesions of the peripheral receptor and effector organs, have not been sufficiently investigated, while the role of the cerebral cortex in these adaptations has not been studied at all. Some preliminary data show that after the amputation of two extremities the functions of standing and walking recover more slowly in young puppies and rabbits than in adult animals (Grigorian, Mirzoian, and Asratian). Apparently this is due to the immaturity of the nervous mechanisms which underlie these functions at this early age.

The significance of the factor of phylogenetic evolution in the development of compensation and in the role played by the higher parts of the central nervous system in the phenomena of compensation, was described in general outline by many early investigators. Although our data concerning the consequences of surgical injury of the spinal cord, peripheral organs and nerves in birds and lower vertebrates, as well as the effect of subsequent removal of the forebrain duplicate to only a slight degree the data obtained by early investigators on the same animals, nevertheless our new data concerning these problems are closely related to these early data. We therefore consider our data concerning the phylogenetic evolution of compensatory adaptations as corroboration, supplementation and further development of the results of early investigations in this direction.

First it should be pointed out that at present we have only limited although thoroughly verified experimental material which shows that the cerebral cortex does not play as important a role in compensation in rabbits as it does in higher mammals. Using the method of electromyography, Shamarina demonstrated in rabbits the following phenomenon: although after the transplantation of the distal tendon of the semitendinosus muscle to the distal part of the removed quadriceps muscle, the transformation of its previous function of flexor of the thigh into the new function of extensor proceeds slowly and gradually, cerebral decortication and even the removal of the nearest subcortical formations do not cause any diminution in the newly developed coordinating relationships.

At the same time it was demonstrated that such a readjustment of functions also takes place when the cerebral cortex in rabbits is previously removed and the tendons of the flexor of the thigh are subsequently transplanted. It must be pointed out, however, that in decorticated rabbits this readjustment of functions proceeds almost twice as slowly as in rabbits with intact brain, which shows that in this case the cortex plays a definite role in the development of compensation.

The experiments of Mirzoian (1956) demonstrated that in rabbits the role of the cerebral cortex in the compensation of functions disturbed as a result of lateral hemisection of the spinal cord is somewhat greater than after the transplantation of the tendons of the muscles; it does not, however, play as decisive a role as it does in dogs. After cerebral decortication in rabbits in which the functions have been compensated after a spinal operation, compensation of the functions of standing and walking disappears, but soon these functions recover.

In birds (pigeons, hens, ducks) amputation of the limbs, transection of the lateral, ventral or dorsal half of the spinal cord, sagittal splitting in the zone of its various segments, deafferentation of the limbs, and extirpation of the cerebellum evoke disturbances of the functions of standing and walking similar to those observed in adult mammals. However, the influence of the removal of the cerebral hemispheres on the restored functions in birds is almost the same as in puppies, kittens and young rabbits: the original compensation disappears but recovers in 3 or 4 months although in a considerably less complete form (according to the data of Karamian, Stefantsov, Dmitriev, Drozdova, Ivanova, and Shoshenko).

In amphibians (frogs) our forms of surgical injury of the spinal cord and of the nerve roots evoke only slight disturbances of the motor and sensory functions of the extremities, while in reptiles (lizards, turtles) they lead to a significant disturbance of these functions which is, however, less profound and prolonged than in birds and mammals. Nevertheless, the compensation of disturbed functions in lower vertebrates is far from reaching the degree of perfection which is characteristic of higher vertebrates. The subsequent removal of the forebrain in frogs does not cause any appreciable effects, while in turtles, and particularly in lizards, it affects only to some degree the state of compensation attained by the organism. A more marked decompensation is evoked in them by the removal of the mesencephalon, after which they do not usually live long (according to the data of Likhina, Vishnevetskaia, Matinian, Dmitriev and Adamian).

It is interesting to note that in birds, amphibians and reptiles the role of the age factor is the same as in mammals (according to the data of Dmitriev, Matinian and Adamian).

The experimental data presented under the above four categories leads to the following very important conclusion concerning the fundamental problem which we are here considering: *In the course of the ontogenetic and phylogenetic evolution of the animal kingdom, the role played by the higher parts of the central nervous system in the development of compensatory adaptations in an injured organism grows steadily, and in higher animals becomes a decisive factor.* It is easy to see that this conclusion fundamentally contradicts Bethe's views on this question.

From the above data it also follows that in the course of the phylogenetic evolution of the animal kingdom two diametrically opposite processes take place. On the one hand, due to the continuously growing differentiation in structure and specialization of the functions of the central nervous organs, injury of their structure evokes increasingly profound disturbances of the functions of the organism; on the other hand, due to the rapid development of the cerebral hemispheres, especially of their cortex, the possibilities for restoration of the disturbed and lost functions also steadily increase. This is a clear manifestation of the dialectics and great creative power of living nature. At the same time this also serves as a source of optimism for those working in the field of rehabilitation of people with various injuries.

The experimental material obtained by us and our collaborators (presented here only in part and briefly), as well as reliable related data obtained by other investigators both past and contemporary, permit us to propose a few general considerations concerning the problem as a whole and especially the physiological mechanisms of the participation of the cerebral cortex, in the development of the adaptations under discussion. Contrary to Bethe's view, the diverse and complex compensatory phenomena in an injured organism are by no means an expression of a variable play of peripheral nervous impulses which are thought to take place in a passive and amorphous central "nervous network," nor are they the result of homogeneous changes in this network which are considered essentially identical in animals of different evolutionary levels. There is every reason to state that the emergence and growth of compensatory adaptations in an injured highly developed organism is a very complex phenomenon which cannot be reduced to a single elementary or even complex physiological process. It is determined by a series of physiological processes which differ in their nature, degree of complexity and effectiveness, and include specifically: the possible regeneration of the injured structures; the training of the uninjured elements and the assumption by them of new functions; the substitutional mobilization of the reserve mechanisms and the intensification of the activity of duplicate mechanisms; the suppression of the activity of the retarding mechanisms; the unconditioned reflex readjustment of the functions of the nerve centers, and especially their conditioned reflex readjustment, which is the climax of this entire complex of the organisms' compensatory measures against the results of its mechanical injury.

Occurring predominantly in the central nervous system, these various processes are differently combined in time and space depending on the character, gravity and localization of the injury, on the level of the phylogenetic and ontogenetic evolution of the organism, etc. This is one of the most striking manifestations of the highly adaptive changeability which is inherent in the activity of the nervous system. One can rightfully say that here, too, i.e. in the development of life-saving compensatory adaptations, living nature manifests its strong tendency towards highly diverse creative activity. These compensatory adaptations differ not only in the character and degree of their complexity, but also in the rate and successive stages of their development. We shall not here go into the details of this question, but shall only point out that in most cases of severe lesions of the central or peripheral organs of a highly developed organism, we observed the following stages or phases in the development of compensatory adaptations, as well as the following features which are inherent in these adaptations.

One of the invariable results of a traumatic lesion of a highly developed organism is a local or diffuse suppression of the functions of certain central organs of the nervous system and of the peripheral receptors and effectors which are connected with them; this suppression may arise in structures located both near the centre of destruction and far from it. The phenomena of such indirect or reflex suppression which are variously known as central shock, depression, diaschisis, asynapsia, reflex paralysis and paresis, etc., have been thoroughly investigated from the phenomenological point of view by clinicians and research workers and are differently interpreted by various investigators. In particular during the last World War, on the basis of Pavlov's ideas we advanced the hypothesis that this suppression is in its origin and nature a supramaximal inhibition which plays a protective and restorative role; it occurs in structures which have been weakened and exhausted as a result of traumatic over-stimulation. This point of view subsequently became widespread among the neurophysiologists and physicians of our country.

The latest achievements of neurophysiology and neurohistology now make it possible more thoroughly to understand the causes and origin of this suppression. We have in mind the data obtained by Eccles (1957) and his collaborators, Brown and Pascoe (1954), Bodian and Mellors (1945), and others, which show that even a simple transection of the neuron axons evokes marked changes in their structure as well as a profound and protracted suppression of their activity and of the synaptic transmission both to and from them. Taking into account the data obtained by these investigators and the peculiarities of the structure of the nervous system as a whole, especially the presence of a dense network of short and long processes of various neurons in this system, one can easily understand the effect which a mechanical lesion of any of its areas, in the center or at the periphery, may bring about in those of its parts which are situated both close to the area of the lesion or far from it, and which are not directly affected by the pathogenic factor.

In any case, the specific role of such indirect central suppression in the general picture of functional disturbances of an injured organism, as well as in the course of subsequent restoration and compensation of functions, is as a rule significant; it depends on the depth, extent and localization of the suppression itself, as well as on the specific typological and age peculiarities of the organism, on its general condition, etc. The liberation of the nervous structures from such suppression is not only essential to the full recovery of their activity, and consequently of the activity of the receptors and effectors which are organically connected with them, but it is also a prerequisite for their subsequent reinforcement by training and for their functional readjustment when this is required by the need to compensate functions disturbed and lost as a result of the destruction of other related structures. In view of the above, the liberation of the intact structures of the central nervous organs from indirect traumatic suppression may be rightfully regarded as the first stage in the process of restoration of disturbed functions in an injured organism.

Numerous laboratory and clinical findings show that in traumatic lesions of the peripheral and central organs of highly developed organisms the phase of suppression of the central nervous system is in most cases succeeded by a phase of heightened excitability if this is not prevented by complicating contributory factors. This phase of heightened excitability of the intact structures of the central nervous system following the phase of their traumatic suppression, is invariably observed in lesions of the cerebral cortex, the spinal cord and other organs of the central nervous system, as well as of the nerve trunks and peripheral organs. This phase is expressed in an appreciable intensification and generalization of the reflex or electric activity characteristic of the given organ and in a weakening of the corresponding inhibitory reactions.

The above can be illustrated by the observation made in Pavlov's laboratories that after the phase of general suppression of the conditioned reflex activity caused by the extirpation of certain cortical zones, the experimental dogs exhibited a considerable intensification of their positive conditioned reflexes and a decline of their inhibitory conditioned reflexes. Not long ago Maksimova demonstrated in our laboratory that the suppression of the electric activity of the cerebral cortex caused by a lateral hemisection of the spinal cord is succeeded by a phase of increased electric activity as compared to the normal level. The heightened reflex activity observed in a transected spinal cord when the phenomenon of spinal shock has passed, has long been known. It has also been quite recently observed after hemisections of the spinal cord (Cannon and Rosenblueth, 1949). The appearance of the phase of heightened excitability in the organs of the central nervous system following the phase of suppression is also observed in cases of clinical and laboratory transplantations of muscle tendons. It appears particularly in the case of the creation of the so-called Krukenberg fingers and transplantation of the tendons of m. sartorius to the patella (Gumener *et al.*, 1958). Ufliand (1956) and his collaborators observed and thoroughly described this phase after different transplantations of muscle tendons in humans and animals. In our laboratory Shamarina, by means of the method of electromyography, demonstrated the presence of this phase in the m. semitendinosus of rabbits, the distal tendon of which was transplanted to the distal tendon of the extirpated m. quadriceps. The heightened activity phase is also invariably observed in the central nervous organs in cases of deafferentation of certain extremities in animals (data obtained by Bickel, Bremer, 1932, Drozdova, and Asratian). A similar phase appears under conditions of a cross-anastomosis of the nerves and is manifested in the so-called phenomena of concomitant movements (Foerster, 1930, Anokhin, and others). It is impossible here to give a comprehensive review and thorough analysis of many other similar clinical and laboratory observations. It may only be pointed out that the phenomenon of heightened excitability in the central nervous organs of an injured organism is probably of a more extensive character and a more complex origin than is the phenomenon of heightened sensitivity of denervated structures. Even the main factors which cause this phenomenon have not yet been discovered or investigated. However, it seems quite probable that a definite role in their occurrence is played by a preceding traumatic suppression.

Although the causes and origin of the heightened excitability phase in the central nervous organs which follows their traumatic suppression have so far not been elucidated, the great significance of this phase in the restoration of the disturbed and lost functions of an injured organism seems to be quite obvious. Both in the activity of the nervous system in general and in this particular case, the state of heightened excitability in the central nervous organs constitutes a basis for the heightened reflex activity of their principal structures, for the mobilization of related structures and their involvement in the accomplishment of the required functions, for the unconditioned and conditioned reflex readjustment of the functions of related and unrelated structures, i.e. the creation of new forms of reflex activity, etc. It may be said without exaggeration that this is the key phase in the entire complex dynamics of the process of compensation of functions. Consequently, the study of the laws of its development in an injured organism, of the factors which determine its degree and duration, as well as of the process of formation of definite types of compensation on this basis, is perhaps one of the most important problems in the field of experimental, clinical and theoretical investigation of the problem of compensation as a whole.

It seems probable that in most, if not all, cases the phase of heightened excitability in the central nervous system organs of an injured organism is also of a temporary character. A gradual transition from this phase to the next phase of more moderate excitability was observed by many investigators and under conditions of various lesions of the organism, particularly lesions of the cerebral cortex (Pavlov and his co-workers), transplantations of the tendons of skeletal muscles (Ufliand, Shamarina and others), cross-anastomosis of heterogeneous nerves (Foerster, Anokhin and others), deafferentation of extremities (Bickel, Drozdova and Asratian), hemisection of the spinal cord (Maksimova, Asratian and others), etc.

The organism may, however, pass from the second to the third phase with different "baggage"; its behavior in the third phase may therefore vary accordingly. If the beneficial conditions of the heightened excitability phase have been utilized to the utmost in the restoration and compensation of the disturbed functions, then in the third phase these restored and compensated functions become, so to speak, "polished" due to the proportioning, greater precision and consolidation of appropriate movements and inhibition of those that are inappropriate. If, however, for any reason the heightened excitability phase has not been sufficiently utilized by the organism to attain a more or less satisfactory degree of restoration and compensation of functions, then, with the transition to the third phase, the chances of their further restoration are greatly diminshed. It must be pointed out that these phases may vary in intensity and duration depending on many circumstances: on the species, age, typological peculiarities and general condition of the organism, on the nature and severity of the lesion, on the environmental conditions, on various factors favoring or hindering the restoration of functions, etc. Due to these circumstances, some of the basic phases may be entirely absent in some cases while in others additional phases may appear; a reversion to a previous phase is likewise possible. We shall here dwell briefly on only one of these numerous questions, since it is of great importance in the problem of compensation as a whole. We have in mind the role of training and exercise in the restoration and compensation of the disturbed functions of an injured organism.

The beneficial effect of exercise on the structure and functioning of the peripheral receptor and effector organs of an intact or injured organism has long been known and noted by many investigators. It is no less effective in relation to the organs of the central nervous system, although here its influence does not always appear in an obvious form, but manifests itself, as it were, in an indirect way. The powerful stimulating effect of exercise on the rate and degree of restoration of functions in an injured central nervous system can be illustrated by a few early and recent laboratory observations. In a number of experiments on monkeys Trendelenburg (1915) evoked a stable paresis of one of the arms by extirpating the corresponding cortical area. A subsequent amputation of the other, intact arm served as an impetus to the frequent use of the paretic arm, to its gradual training and, in the end, to the restoration of its functions. In similar experiments Franz and Ogden (1917–1918) achieved the same result merely by immobilization of the intact arm of the monkey instead of its amputation. Woolsey (1956) demonstrated such a heightening of functions by training even in decorticated monkeys. Due to systematic exercise of the reflex activity and to massage of the skeletal muscles, these monkeys recovered the functions of standing and walking which, according to the data of other investigators (Karplus and Kreidl, 1914; Fulton and his collaborators, 1946) they cannot achieve after such an operation unless they are especially trained. Nesmeianova (1956) demonstrated in our laboratory that even the reflex activity of a transected spinal cord can be appreciably intensified by training. These laboratory observations can be corroborated by numerous early, but especially recent, clinical data which demonstrate that exercise (in the form of various kinds of medical gymnastics, work therapy and other methods of training) exerts an especially favorable influence on the restoration of disturbed functions of the cerebrum, cerebellum, spinal cord and other injured organs of the central nervous system, and that the functions of these organs can be markedly heightened by training.

It must be pointed out, however, that until recently both clinicians and experimenters could evaluate the heightening of functions which occurs in the central nervous organs as a result of training only by means of certain indirect indices and knew very little of the physiological basis of this phenomenon. The recent precise experiments of Eccles provide not only direct demonstrations of the existence of such heightening of functions, but also data on its physiological basis. Several weeks after the transection of the posterior roots of a number of segments distal from the intervertebral ganglia, there occurs a marked intensification of the reflex reaction from the intact higher posterior roots. Eccles calls this phenomenon "compensatory reaction" and ascribes its development to the forced intensive usage of these roots. On the other hand, the reflexes of the deafferentated segments become considerably weakened, which Eccles explains as due to the forced inaction or disuse of their nervous elements.

These and other observations taken together give sufficient reason to believe that the heightened excitability phase can be prolonged in the injured central nervous organs by means of their sytematic exercise or reflex stimulation if this phase has not yet passed; when it has passed, a condition of prolonged and heightened excitability can be created *de novo* in these organs. There are also certain reasons to believe that, in contradistinction to the extensive and generalized character of the heightened excitability observed in the central nervous organs in the phase which follows that of traumatic suppression, the heightened excitability evoked in these organs by training is of a more localized character. It should also be pointed out that in this case it is not a question of some specific characteristic of the injured central nervous system; here we have a particular manifestation of a general law which governs the activity of this system and of all other excitable tissues, namely, their ability to develop a state of persistent heightened excitability under conditions of a systematic flow of beneficial nervous impulses towards them. Not only active movements of parts of the body but also passive movements and even a mere massage of individual parts, may give rise to impulses which are transmitted to the central nervous structures.

In conclusion, I should like to say a few words concerning our interpretation of the mechanism which underlies the decisive role of the cerebral cortex in the compensatory adaptations in adult higher animals, i.e. the mechanism of the phenomenon which we have investigated in connection with this particular problem.

The data obtained by us and our collaborators, as well as by some other investigators, concerning the existence of cortical representations of unconditioned reflexes and their active participation in the accomplishment of these reflexes, give sufficient reason to believe that this form of cortical activity plays a significant role in the development of compensatory adaptations. We believe, however, that in higher animals and man the decisive role of the cortex in the development of these adaptations is, in the main, accomplished by means of a conditioned reflex readjustment of functions. This is demonstrated not only by the possibility of elaborating motor conditioned reflexes to injured limbs, but also by the whole dynamics of the development of compensatory adaptations which have all the attributes peculiar to the elaboration of new motor habits and to learning in general.

What is then our idea of the inner aspect of this problem?

In the light of modern achievements of neurohistology and neurophysiology concerning the structural and functional connections and interrelations between the cerebral cortex and other parts of the central nervous system, we may give the following rough description of our ideas concerning the structural and functional bases underlying these two forms of cortical readjustment of functions in an injured organism.

The spinal cord and medulla oblongata, which are the chief central organs of primary reflex activity, are projected onto the cerebral cortex as onto a screen by means of ascending and descending conducting systems. We do not regard this projection as a mass of discrete receptor and effector representations, which is a commonly accepted concept, but as representations of reflex arcs with all their central elements (Fig. 23). It is taken for granted that these cortical representations of highly diverse reflexes, like the primary reflex arcs of the spinal cord and medulla oblongata, have a close interconnection and interaction. When the organs of the central nervous system, nerves, or receptor and effector organs are injured, all the local phenomena which appear in this connection, including the above-mentioned phasic conditions, are adequately reflected in the respective structures of the cortical projections of the injured reflex arcs; this is effected by means of the corresponding afferent systems and is probably also due to the antidromic influence of the efferent pathways. It is even possible that in the cortical structures of the reflex arcs, which are the newest, most reactive and plastic structures of the entire central nervous system, these phases are of a particularly pronounced character.

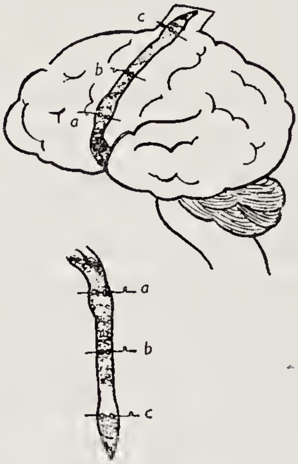

FIG. 23. Diagram illustrating projection of the spinal cord in the cerebral cortex.

Under these conditions the persistent heightened excitability of the cortical structures which follows the phase of traumatic suppression or is produced by exercise, will play a double role in the process of compensation. On the one hand, such excitability at the cortical level of the injured reflex arcs could cause an intense activity of the corresponding cortical structures and will simultaneously create a favorable background and preparation for the activation of the reserve structures and for their reinforcement by training; this will at once influence the lower structures of the reflex arcs and will be expressed in corresponding reflex actions. On the other hand, the persistent and more or less localized (as a result of training) heightened excitability of the cortical structures of the reflex arcs may serve as a basis for the coupling of the conditioned connections between these structures, as well as between other near and distant points of the cortex which have simultaneously become excited. This conditioned reflex mechanism of critical readjustment makes it possible to involve the cortex as a whole, with its tremendous potentialities, in the process of restoration and compensation of the disturbed functions of an injured organism. If, moreover, we take into consideration the important role of kinesthesia in the motor activity of a highly developed organism, as well as the bidirectional conditioned connections inherent in motor conditioned reflexes, we shall more fully appreciate the inexhaustible potentialities of conditioned reflex compensation in the reconstruction of the motor functions of an injured organism, i.e. a radical readjustment of the inborn or previously acquired forms of coordination and the creation of new forms in accordance with the new requirements of the organism. At the same time we shall understand more thoroughly the role of training and practice in the compensation of functions. Their role is by no means confined to reinforcement of the heightened excitability already present in the corresponding nervous structures, or to the re-creation in them of such a condition. They are also an inexhaustible source for the formation of ever new forms of coordination.

Furthermore, according to modern neurophysiology there is a circular interaction between the central nervous organs and both the peripheral effectors and the peripheral receptors. This is deduced from well known early findings concerning the existence of proprioception and from a number of new findings which indicate the influence of the central organs on the condition and functioning of the peripheral receptor apparatus. We refer to the results obtained by Orbeli (1935) and his co-workers concerning the possibility of changing the condition of the peripheral receptors through the symphathetic nerves, i.e. through one of the efferent pathways of the central nervous system. We also have in mind the data of Granit (1956) and other investigators which demonstrate the existence of a centrifugal (feedback) influence of the central nervous organs on the condition and functioning of a number of receptors. Without going into the details of this question, we may point out that in the light of these findings and of other achievements of modern neurophysiology mentioned above, we can reasonably believe that training can contribute to the process of development and perfection of compensation in an injured organism by activating these beneficial circular interactions between the central and peripheral organs. The intensification and perfection of the activity of the central, and especially the higher, structures, may effect an improvement in the condition of the peripheral receptors and effectors, and, as it were, fertilize their activity. The intensification and perfection of the action of these peripheral organs may in their turn exert a beneficial reciprocal influence on the condition and activity of the central structures.

To illustrate what has been said above concerning our interpretation of the mechanisms which determine the role of the cerebral cortex in the development of compensatory adaptations in an injured organism, we shall refer to a specific example of such compensation after a lateral hemisection of the spinal cord, and give a schematic presentation of our basic idea. Our choice of this particular form of lesion for illustrative purposes is largely due to the fact that the results of a lateral hemisection of the spinal cord, as well as the process of development of compensation and the role of the cerebral cortex in this process, have been thoroughly studied by many scientists in numerous experiments, but the interpretations of the findings are markedly contradictory.

There are sufficient morphological and functional reasons to believe that a lateral, e.g. right, hemisection of the spinal cord interrupts not all, but only the main pathways of the bidirectional contact between the brain and the right half of the spinal cord situated caudal to the line of transection (Fig. 24, I, A and P). The secondary pathways of this connection, which pass through the uninjured left half of the spinal cord, remain intact. Such are, for example, the direct pyramidal pathway whose axons pass to the opposite side at the level of the segment (P^1), the extrapyramidal pathways (Ep), and the lateral spinothalamic pathway (St), which also passes to the opposite side at the level of the segment. There are also undoubtedly other effective circuitous, and probably more polysynaptic and reserve descending and ascending pathways. The existence in higher animals of such a circuitous functional connection between the organs of the brain and the lateral half of the spinal cord soon after its hemisection is demonstrated by a number of findings which indicate the development of decerebrate rigidity in the extremity which is innervated by this section of the spinal cord as well as the participation of this extremity in tonic neck reflexes (Mandoki and Obrador).

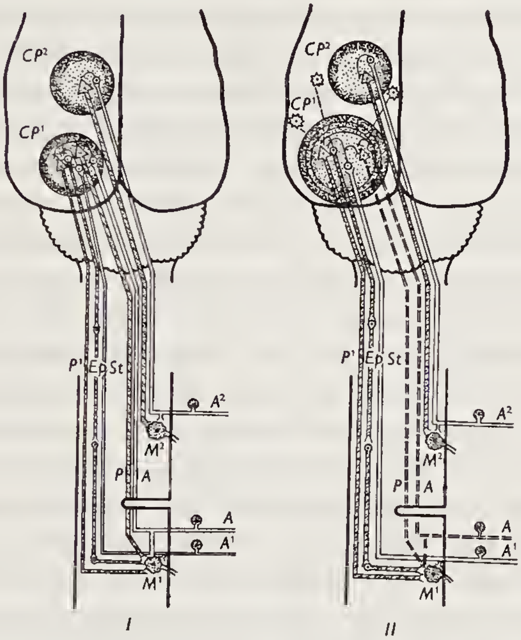

FIG. 24. Diagram illustrating injury of the conducting pathways of the spinal cord caused by a lateral hemisection (I) and the participation of the cortex in the compensation of functions (II).

In spite of the existence of these effective circuitous pathways, the supporting and locomotor functions of such an extremity during the immediate postoperative period are profoundly disturbed and do not recover for a long time. From this it follows that the circuitous pathways are not fully effective and that only with the lapse of time do they, together with the activated reserve pathways, gradually acquire the ability to effect a complete functional connection between the organs of the brain and the caudal part of the spinal cord on the side of the lateral hemisection. Although under these conditions the heightened sensitivity of the nerve cells which is observed in this half of the spinal cord as a result of decentralization may play a definite role, still this is not the only mechanism as is assumed by Rosenblueth; it is not even the main mechanism. If heightened sensitivity were the only, or even the principal, factor, then after such "decentralization" as cerebral decortication, the already developed compensation should become intensified and not disappear as actually occurs in adult higher animals; or else after hemisection of the spinal cord this compensation would develop much better in previously decorticated than in normal animals, which, however, does not occur. Our data clearly show that it is the cerebral cortex which plays the decisive role in the re-formation of these circuitous pathways in adult higher animals, and that this is probably accomplished by means of certain mechanisms, which are presented schematically and in simplified form in Fig. 24 II. Due to a number of circumstances already mentioned, the level of excitability of the cortical point of an affected extremity is much higher than that of adjacent, and especially remote, points (in Fig. 24 II this is schematically shown as rings CP^1). On the one hand, this condition greatly intensifies the activity of the circuitous pathways (in Fig. 24 II this is indicated by thick lines) and activates the reserve circuitous pathways; on the other hand, it constitutes a basis for the formation of new conditioned connections (dotted lines between CP^1 and the star shapes) and for the above-mentioned conditioned reflex readjustment of functions. It is possible that certain changes, similar to those which were mentioned earlier (an increase in the excitability of the intact nervous formations, their reinforcement by training, etc.), take place directly in the zone of injury and that these changes contribute to the process of restoration of the disturbed functions. However, it seems to us that in adult higher animals and in man these local changes play a secondary role compared with the processes which occur in the cortex.

In the light of the above findings and hypotheses one can understand and explain some early and recent enigmatic and contradictory data concerning this problem. We have in mind the experiments of Mott (1892) and the comparatively recent experimental investigations of Mettler, as well as of Mandoki and Obrador; they stimulated the motor zones of the cerebral cortex in dogs and monkeys which had previously been subjected to a lateral hemisection of the spinal cord and which subsequently recovered the disturbed functions. An electric stimulation of the motor zones of the cortex applied in the course of these experiments did not as a rule evoke any movements of the extremities on the side of the hemisection and below its level. Such movements were occasionally observed only in the experiments of Mott.

If we assume that the restoration of functions is here determined mainly by the formation of new conditioned connections in the cortex, it can easily be understood that under the conditions of such experiments it is very difficult or even impossible to demonstrate the function of these conditioned connections, which are characterized by extreme lability and vulnerability to various changing factors. Moreover, under the conditions of these experiments the heightened excitability which is caused by training must considerably weaken if not disappear altogether. We have frequently observed that animals with strongly pronounced compensatory adaptations exhibit a considerable decompensation of function in the presence of various infectious diseases and new traumata, under the action of narcosis, and sometimes under the influence of a deterioration in the general condition of the organism due to inadequate care of the animals.

It is understood that all we have said concerning the mechanisms of the participation of the cortex in the achievement of compensatory adaptations in an injured organism is still largely a hypothesis which is based predominantly on indirect evidence and requires direct, thorough and exact experimental verification. However, in our opinion there are certain reasons to believe that this hypothesis even now has definite advantages over others in the interpretation of data concerning the problem we are considering here.

In conclusion, we should like to point out that in investigating this problem, we proceeded from the ideas of Pavlov and were guided by them. We are happy that the main results of our work fully accord with Pavlov's teaching, particularly with his fundamental hypothesis that in a highly developed organism the cerebral cortex is a very powerful organ which effects all the complex relationships with the environment, an organ of extremely delicate, precise and perfect adaptation to the environment.

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and followers, I. S. Tsitovich (1913), K. M. Bykov (1943), L. A. Orbeli (1945), Gantt and Hoffman (1940), Hargins and Mann (1925), and others, accumulated abundant and varied data showing that in higher animals and man conditioned reflexes can be elaborated for the activity of all the external and internal organs and systems of the organism, or at least for all those functions of a highly developed organism which were especially investigated from this point of view.

Is the elaboration and achievement of conditioned reflexes the only means or the only physiological mechanism by which cortical regulation of the various functions of the organism is accomplished, or does the higher part of the central nervous system also regulate these functions by some other mechanism?

A general answer to this question was given by Pavlov almost half a century ago in his new theoretical concept of the nerve centre as a system or constellation of central nervous formations or points located in different parts of the central nervous system, including the cerebral cortex, formations which are closely interconnected both structurally and functionally, and which constitute a single functional system and regulate certain functions of the organism. From this theoretical proposition it follows that the cerebral cortex, due to the presence in it of a component or representation of such a complex nerve centre, participates in the regulation of various functions of the organism not only by means of a conditioned reflex mechanism, but also by some other mechanism.

Later Pavlov revised his views on the localization of the coupling of conditioned connections, i.e. on the localization of conditioned connections in the cerebral organs, and advanced his famous proposition concerning the representation of unconditioned reflexes in the cerebral cortex. This profound theoretical proposition, which represented a development of his interpretation of the essence of a nerve centre, gives a more definite and clear answer to the above question on the forms and means of cortical regulation of the organism's various functions. According to this proposition, each unconditioned reflex is represented in the cerebral cortex by a definite point which becomes excited as a result of the stimulation of a corresponding receptor. When the excitation of this point repeatedly coincides in time with the excitation of other points of the cortex, a conditioned connection is established between all these points and gives rise to a conditioned reflex.

Thus, the proposition that there is a cortical representation of unconditioned reflexes, led to the renunciation by Pavlov of his previous concept of the localization of conditioned connections in the cerebral structures of a highly developed organism, and to his proposing a new idea on this extremely important question. Whereas he had previously held that a conditioned connection is coupled between the cortical points of the so-called "indifferent" stimuli and the subcortical centres of the unconditioned reflexes, i.e. between different cerebral organs, according to his new view the conditioned connection is coupled between different points of the cortex and is located entirely within the cerebral cortex, within the limits of its own structures.

This profound and progressive concept, which fully accords with other recent advances in the field of the physiology and morphology of the cerebral cortex, has rapidly gained general recognition. Until recently, however, the necessity for further experimental and theoretical investigations of Pavlov's proposition concerning the cortical representation of unconditioned reflexes has been almost entirely disregarded.

Pavlov based his proposition on the observation that in conditions of the so-called summation of similar and equivalent conditioned reflexes, i.e. during the simultaneous action of two or more positive conditioned stimuli of the same modality, the combined conditioned effect is far short of the arithmetical sum of the magnitudes of the conditioned reflexes caused by the application of each separate stimulus, and often amounts only to the effect of the strongest stimulus. For example, if conditioned stimulus A evokes a reflex equal to 30 units, and conditioned stimulus B a reflex equal to 20 units, the simultaneous action of these two stimuli can lead to a reflex of only 35 units, and not of 50 units as might be expected. In other words, although volleys of impulses come to the nerve point of the unconditioned reflex from the points of two or more simultaneously acting conditioned stimuli along conditioned connections which converge in this nerve point, these impulses do not evoke an excitation of a magnitude equal to their sum.

Pavlov believed that this phenomenon could be satisfactorily explained only if we assume that the conditioned connection is coupled between two points of the cortex and that the point of convergence of the conditioned connections is located in the cortex, i.e. in an organ whose cells are generally characterized by a relatively low working capacity, because of which this point is unable to produce a high total output when volleys of impulses come to it simultaneously from several sources. This is schematically shown in Fig. 1A. The cortical points of conditioned stimulus CS^1 and of conditioned stimulus CS^2 are connected with the cortical point of unconditioned reflex UR. If the nerve point of the unconditioned reflex with which the conditioned connection is established were located in the subcortical formations, as Pavlov at one time believed, then during the simultaneous action of two or more similar positive conditioned stimuli an actual sum of the separate conditioned effects would take place; this would be explained by the fact that such a nerve point, due to the high working capacity inherent in the cells of the subcortical formations, would be able truly to summate the simultaneously arriving excitatory volleys from several cortical points of conditioned stimuli. This is schematically illustrated in Fig. 1B. The cortical points of the same conditioned stimuli CS^1 and CS^2 are connected with the subcortical point of unconditioned reflex UR.

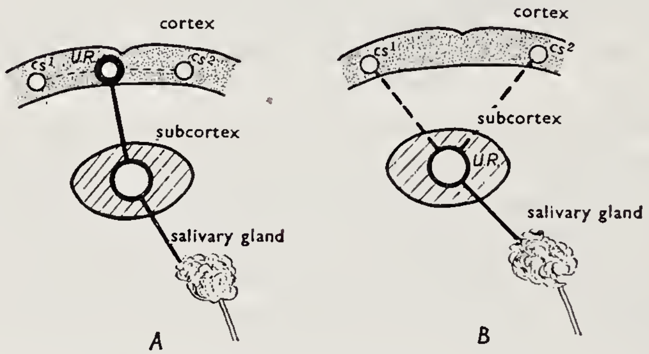

FIG. 1. Diagram illustrating the cortical representation of the unconditioned reflex.

Thus, although Pavlov convincingly supported this new proposition, still it was necessary further to substantiate experimentally the proposition that there exists a cortical representation of unconditioned reflexes and to discover and investigate its role, its characteristics and the laws of its functioning, as well as further to define theoretically and to advance Pavlov's proposition. There was also the alluring prospect of utilizing this profound idea of Pavlov for the elucidation of many other complex and intricate problems of modern physiology of the cerebral cortex.

It must be pointed out that among the abundant experimental data regarding the physiology of the cerebral cortex obtained by scientists in the last, but especially in the present, century, there are many which indicate the existence in the cerebral cortex of a highly developed organism, a representation of individual receptor and effector organs and systems; these data also show that in the course of the evolutionary development of mammals there occurs an ever increasing corticalization of various functions. These data, which provide a basis for the development by many investigators of various theoretical concepts regarding certain aspects of the activity of the cerebral cortex, can undoubtedly help to strengthen the experimental basis of Pavlov's theoretical proposition concerning the cortical representation of unconditioned reflexes. This applies to numerous data which have been obtained from experiments with partial or total extirpation of the cerebral cortex; from the electric or chemical stimulation of the cortex during acute and chronic experiments on animals, or during surgical operations on the human brain; from experiments with recording of the electric activity of the cortex, particularly of evoked potentials of its separate structures; from experiments with the antidromic stimulation of efferent cortical nerve cells, etc.

I cannot here consider this vast problem in greater detail, nor support the above statements by concrete examples, but shall later cite some examples which have a special relation to our investigations connected with this problem. Here I wish only to point out that, no matter how important theoretical argument in science may be, it can never replace specific experimental research in a given area, let alone abolish the need for such research.

Special investigations have recently been carried out in a number of laboratories of the Soviet Union by Pavlov's pupils, using different methods. Among these the investigations of P. S. Kupalov (1951) and his co-workers, conducted over the course of many years, must be mentioned first. Until recently these investigations concerned the question of the existence and role of the cortical representation of unconditioned reflexes. The investigations were carried out by comparing the magnitude and character of unconditioned alimentary reflexes evoked in one instance by the application of unconditioned stimuli alone, and in other cases by the application of the same unconditioned stimuli after conditioned stimulations of various durations. These workers demonstrated particularly that a concentrated sugar solution placed in the mouth of a dog evokes considerably less reflex salivation than when administration of the same amount of sugar solution of the same concentration is immediately preceded by the application of an adequate conditioned stimulus. This phenomenon is explained as follows: the conditioned stimulus increases the excitability of the cells which enter the cortical representation of the unconditioned reflex, and the unconditioned stimulus (sugar solution) acting on this background evokes a stronger unconditioned reflex.

Over the course of many years our laboratory has also been engaged in special and systematic investigations of this question. We have chosen an entirely different experimental method, namely, that of extirpation of the cerebral cortex with subsequent study of the resulting changes in the unconditioned reflexes and functions of the organism. It should be pointed out that this old and well-tried method was never before applied to special and systematic investigations of this problem, except for isolated observations carried out by G. P. Zelenyi *et al.* (1913) on the secretion of gastric juice in decerebrated dogs using a method of sham feeding (mastication of meat wrapped up in gauze) which does not exclude the possibility of food entering the stomach, and except for similar observations of D. S. Fursikov *et al.* (1928) on the secretion of saliva in dogs after extirpation of the cerebral cortex.

Although the main defects of the method of partial or complete cerebral decortication for the solution of different physiological problems were well known to us, not only from various sources in the literature, but also from our own practical experience acquired over the course of many years, nevertheless we gave preference to precisely this experimental method of investigation because by this means we could obtain data which made possible a direct approach to the solution of the problem in question.

Our initial observations in this field were made in 1934 and 1935. In order to investigate the role of the cerebral cortex in the compensation of the functions of an injured organism, we removed the cerebral cortex both in normal dogs and in those in which, long before this extirpation, the extremities, receptors, nerves, roots of the spinal nerves, spinal cord, etc., had been surgically injured. These experiments, the basic results of which were described in Chapter 2, were carried out on many dogs (about 100) which had been deprived of the cerebral cortex and which survived for many months and even years (Asratian, 1953).

Our observations showed that removal of the cerebral cortex essentially modifies the nature and course of unconditioned reflexes both in normal and in previously operated dogs. Highly significant in this respect are the righting and locomotor reflexes. It has been known since the classic experiments of F. Goltz (1892) that these reflexes persist in decorticated dogs; but although according to the data of Goltz, Rothmann (1923), Zelenyi (1930), Rademaker (1931), Bard and Rioch (1937), Popov (1953), Klasovskii (1935), as well as our data (Asratian, 1938), these reflexes persist after the removal of the cerebral cortex, this does not mean that they remain unchanged. As demonstrated by our observations carried out over the course of many years on a large number of decorticated dogs, these reflexes undergo marked changes after the removal of the cerebral cortex; they become coarse, sluggish and incomplete. The same is true of many other somatic and vegetative reflexes which can be observed under ordinary laboratory conditions.

Considering the importance and urgency of this matter, not only in the problem of compensation, which is the subject of our investigation, but also in the entire physiology of the central nervous system and especially of its higher parts, we decided to change from the usual and often superficial laboratory observations to a special, systematic and thorough study of these phenomena. We started such investigations in 1938 and 1939 and, after a long interval due to the War, we have now resumed them and are conducting them at an ever increasing rate.

Our experimental methods and technique are briefly as follows: in normal animals, chiefly in dogs, we first study as thoroughly as possible certain unconditioned reflexes or functions of the organism. Then the cerebral cortex of the experimental animal is extirpated in two successive aseptic surgical operations, after which the same unconditioned reflexes and functions of the organism are studied for a period of several months (sometimes even a year or more). In most cases we completely remove the cortex of both cerebral hemispheres in our experimental animals, but in some cases, when it is necessary to investigate the reflexes or functions of symmetrically paired organs (salivary glands, extremities, etc.), or of the blood vessels and skin of symmetric parts of the body, we remove the cortex of only one hemisphere. A comparison of the data obtained before and after the cerebral operation makes it possible to discover the resultant changes in the intensity, character and dynamics of the reflexes or functions of the organism under investigation, and on the basis of these observations to determine whether the cerebral cortex participates in the accomplishment of these reflexes and functions, the character and physiological significance of this participation, etc. When the functions of paired organs are studied after the removal of the cortex of only one hemisphere, this also can be accomplished by comparing the data which concern the injured and the intact organs of the experimental animal.

The investigations which we carried out with our collaborators on numerous dogs (of which more than 30 were bilaterally decorticated), as well as on a number of rabbits and birds, showed that total cerebral decortication (in birds, the removal of the forebrain) causes significant and fairly stable changes in the intensity and character of many somatic and vegetative reflex reactions of the organism, as well as in the neuro-humoral regulation of some of its complex functions. These changes, however, are not uniform. All the reflexes which we investigated can be arbitrarily divided into two groups, according to similarity of the resultant changes.

In the first group we include reflex reactions which become considerably weakened as a result of cerebral decortication, i.e. which decrease in intensity and sometimes in duration and become less perfect and less adaptive.

Specifically, this group includes the following reflex reactions. The early experiments of Ia. M. Pressman (1941), and particularly the recent experiments of T. A. Mal'tseva (1957) on dogs with chronic fistulae of the ducts of the symmetric parotid, sublingual or submaxillary salivary glands, showed that cerebral decortication reduces by almost one half the reflex secretion of saliva both to various foods (bread, meat, dried bread, dried meat) and to various inedible (rejected) substances (dilute acids, alkalis, etc.). It has, moreover, been demonstrated that although in decorticated animals the quantity and quality of the reflexly secreted saliva depend on the kind of food presented, on its quantity and degree of dryness as well as on the kind, concentration and quantity of the inedible (rejected) substance, this adaptability of reflex salivation is less pronounced in these than in normal animals.

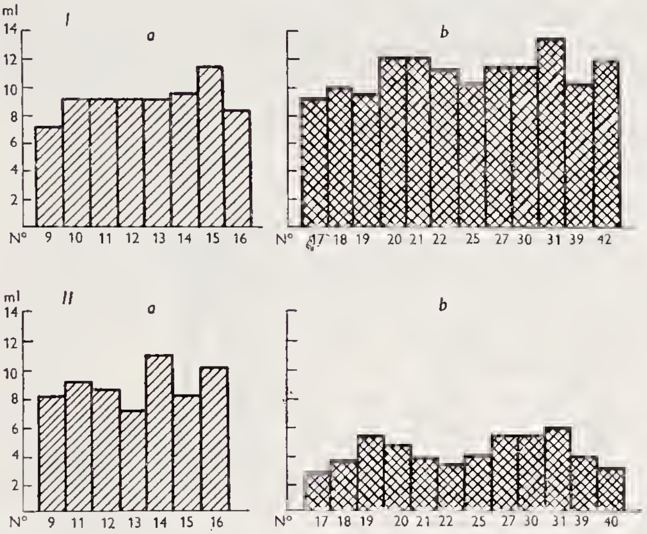

FIG. 2. Quantity of reflex secretion of saliva in ml (bars) to 30 g of dried bread in a dog before and after left unilateral decortication. I, right parotid gland; II, left parotid gland. (a) before the operation; (b) after the operation.

The changes which take place in the secretory activity of the salivary glands as a result of cerebral decortication are still more distinct when we remove the cortex of only one hemisphere in the experimental dogs (experiments of Mal'tseva). After decortication of one hemisphere the reflex secretion of the parotid and other salivary glands of the left and right sides, which is characteristically symmetrical in intact animals, becomes markedly asymmetrical. As a result of the action of the same edible or rejected substances upon the taste receptors, the amount of saliva secreted by the salivary glands of the operated side is smaller by almost one half than that secreted by the salivary glands of the opposite side, i.e. of the side on which the cerebral hemisphere is intact (Fig. 2). It should be pointed out that this asymmetry in the activity of the salivary glands of the operated and intact sides is observed, although in a somewhat less pronounced form, even two or three years after the operation. Similar data were obtained by E. Martinek (1956) and K. S. Abuladze (1956) in Kupalov's laboratory.

The investigations of A. A. Markova (1957) showed that cerebral decortication in dogs results also in certain changes in the activity of the gastric glands similar to the above-described changes in the activity of the salivary glands. By means of chronic experiments on dogs with oesophageal transections and gastric fistulae, Markova demonstrated that in so-called sham feeding, decorticated dogs not only exhibit a considerable decrease of the reflex secretion of gastric juice to meat and bread compared to normal dogs, but also demonstrate marked changes of specificity in the dynamics and character of gastric juice secretion in response to sham feeding with different foods (meat, bread and milk). Figure 3 shows that all these three different types of food evoke in decorticated dogs a more or less uniform type of reflex secretion of gastric juice.

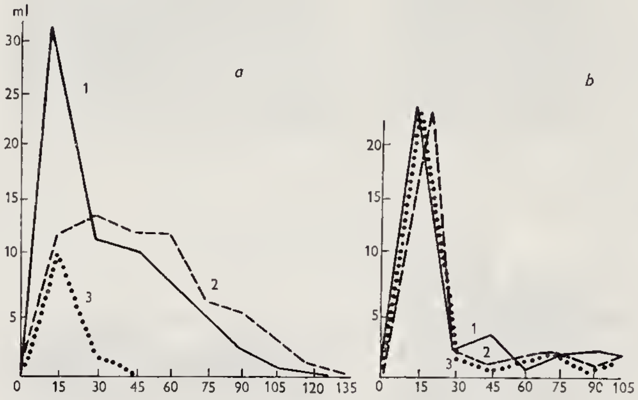

FIG. 3. Dynamics of reflex secretion of gastric juice in a dog during sham feeding with meat (1), bread (2), and milk (3). (a) normal; (b) after total cerebral decortication.

According to the experiments of N. S. Dzhavadian (1956), total decortication also leads to profound changes in the dynamics and adaptability of the complex of interoceptive cardiovascular reflexes which ensure a relative constancy in the level of arterial pressure in normal organisms in different situations, including moderate losses of blood. Dzhavadian, in full agreement with the data of many other investigators, showed that in normal dogs a phlebotomy performed at a moderate rate and amounting to one or even two per cent of the body weight, does not appreciably affect the arterial pressure or the general state of health. Unilateral decortication does not change the picture to any appreciable degree. However, in bilaterally decorticated dogs a phlebotomy performed at the same rate and amounting to as little as 0·4 or 0·5 per cent of the body weight results in a considerable and stable decrease in arterial pressure. When the hemorrhage amounts to 0·9 per cent of the body weight it results in the rapid death of the animal (Fig. 4).

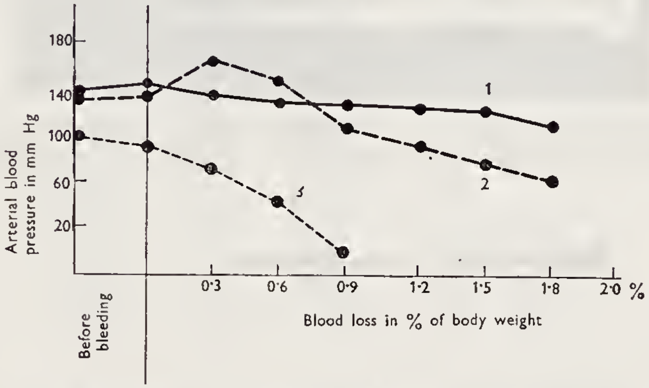

FIG. 4. Changes of arterial pressure in dogs as a result of hemorrhage: normal (1), after unilateral decortication (2), after total decortication (3).

Our co-workers obtained data showing that after bilateral decortication, the locomotor and tendon reflexes of the extremities become weakened. These changes in the reflexes of the symmetric extremities, just as in the case of the symmetric salivary glands, are especially marked after the extirpation of the cortex of only one hemisphere; due to the marked dominance of nervous cross connections, the contralateral extremities of the dog are chiefly affected and therefore the symmetric unaffected extremities may serve for control purposes. In a series of such experiments performed on dogs, B. D. Stefantsov (1952) demonstrated that the flexor reflex of an affected hind extremity becomes considerably weakened in intensity and particularly in stability (Fig. 5). By means of rhythmic electric stimulation of the paw of the affected extremity this reflex can be evoked much more quickly than can the same reflex of the unaffected symmetric extremity stimulated in the same way. Analogous data concerning the knee reflexes have recently been obtained by E. A. Romanovskaia

(1957) on unilaterally decorticated rabbits (Fig. 6). In other words, in both dogs and rabbits the motor reflexes of the extremities contralateral to the injured cerebral hemisphere become fatigued much sooner than the same reflexes of the control extremities.

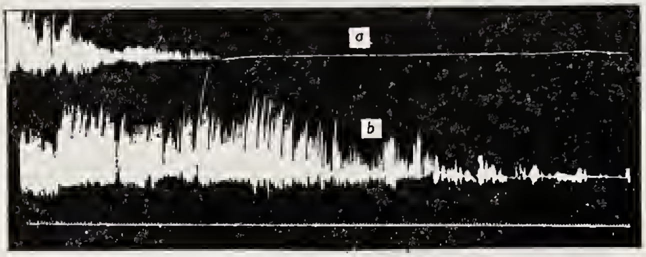

FIG. 5. Kymogram of fatigue of the flexor reflex of the right (a) and left (b) hind extremities in dogs after left cerebral decortication.

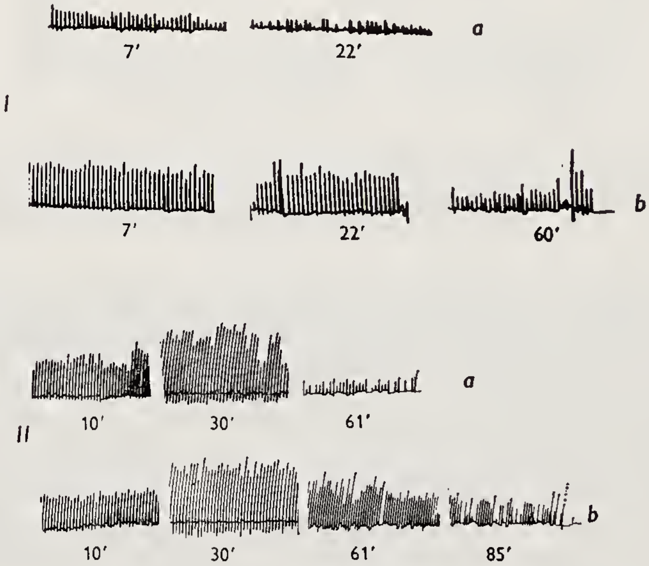

FIG. 6. Kymogram of the knee reflex in a rabbit: (a) left extremity, (b) right extremity, 20 days after right cerebral decortication (I), and 3 months after this operation (II).

Along with the changes in the group of reflexes described above, which result from extirpation of the cerebral hemispheres, definite changes also take place in a group of other, more complex functions of the organism which are probably controlled largely by the nervous system. This group includes the function of maintaining relative constancy of volume and of chemical and morphological composition of the circulating blood; the absorption from the gastrointestinal tract; the function of the sex organs; the reaction of local vasodilatation and of increase in vascular permeability. According to the data obtained by our collaborators, after cerebral decortication all these functions also are greatly weakened and become less perfect and less adaptive. The above-mentioned experiments of Dzhavadian demonstrated that after this operation the ability of the animals rapidly to mobilize their reserve blood and tissue fluid under conditions of loss of blood considerably diminishes, because of which their arterial pressure decreases rapidly and the circulation becomes disturbed. Moreover, the process of erythropoiesis also becomes considerably weakened in these animals. Dzhavadian demonstrated that even a comparatively insignificant anemia caused by loss of blood during decortication persists for a long time. An anemia intentionally provoked in these dogs by removing a relatively small amount of blood (equal to 0·6 per cent of the body weight) cannot be altogether overcome by the animals, and they die within two or three weeks.

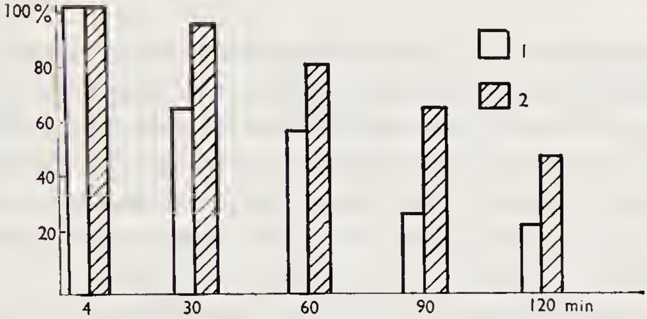

FIG. 7. Changes in concentration of Congo red in the blood of dogs: in normal animal 1, (clear bars), after total cerebral decortication 2, (striped bars), at different periods after its introduction. The concentration of the dye in a certain portion of blood 4 min after its injection is taken as 100 per cent.

The decline in the ability of decorticated dogs to restore the disturbed composition of their blood is also indicated by the results of a number of experiments performed by S. A. Chesnokova (1957), which showed that infused Congo red is eliminated from the blood of decorticated dogs much more slowly than from that of normal dogs (Fig. 7). Similar data, using the introduction of salts of ordinary or radioactive calcium into the blood, were obtained by V. S. Kulikova (1956) in experiments performed on decorticated dogs. This characteristic, as well as a decrease in the process of intestinal absorption in decorticated dogs, was also demonstrated by the experiments of I. K. Zhmakin (1957). He introduced definite amounts of methionine with labelled sulphur into the stomachs of normal and decorticated dogs and demonstrated that the methionine is absorbed into the blood and excreted more slowly in decorticated than in normal dogs.

Highly illustrative also are changes in the dynamics of alimentary hyperglycemia which appear after cerebral decortication. The experiments performed by V. S. Kulikova on dogs and rabbits showed that after the administration of a definite dose of glucose (5 g/kg of body weight) the blood sugar levels in decorticated animals considerably exceed the initial levels and persist much longer than in intact animals.

Other experiments carried out by Chesnokova (1957) show that in decorticated dogs the complex vascular reaction, which consists at least of a local vasodilatation and of an increase in vascular permeability, is considerably retarded compared with that in normal dogs. This was discovered by means of a special method developed by Oivin and Monakova (1953), which involved the introduction into the blood of the experimental dogs of definite amounts of trypan blue and subsequent treatment of a small area of the skin on the animals' sides (previously cleaned of hair) with xylol. Most of the experiments performed by Chesnokova showed that the blue spot on the area of skin subjected to this treatment (this spot being the indicator of the reaction) appears much later in decorticated than in normal dogs. This difference is particularly apparent in symmetric areas of the skin of dogs which have been deprived of the cortex of only one hemisphere: in the area contralateral to the operated hemisphere this complex vascular reaction appears after considerable delay and develops more slowly than in the symmetric skin area on the other side. For example, whereas in intact dogs the dye appears in the treated area of the skin 3–5 min after its introduction into the blood, in decorticated dogs it appears only in 4–10 min.

Similar data were also obtained by Chesnokova regarding the permeability of the hemato-ophthalmic barrier. Using fluorescein as an indicator of permeability (Erlich's method), she found that the permeability of the hemato-ophthalmic barrier of the ipsilateral eye, and often of the contralateral eye, considerably diminishes in rabbits after decortication of one cerebral hemisphere. After decortication of the second hemisphere in these animals the decline of permeability of the hemato-cephalic barrier of both eyes becomes extremely severe. For example, while in the case of intact rabbits fluorescein injected into the blood appears in the anterior chamber after a period of 9–12 min, in decorticated rabbits it appears only 25–30 min after its injection into the blood.

We also obtained some preliminary data concerning the functioning of the sex organs in decorticated animals. In the course of many years of experimentation we have never observed the phenomenon of natural erection in decorticated male animals, but it was possible in some to evoke erection and ejaculation artificially, by means of a slight massage of the penis. Among the decorticated females, some failed to show evidence of seasonal estrous changes. Of those which did demonstrate these changes, some were mated with normal males during the period of heat, but only one of the females became pregnant. In view of the extreme weakness of the complex of parturition reflexes in these females, artificial measures had to be taken; this, however, did not save the lives of two puppies which, judging by their appearance, had reached normal intrauterine development. At present we are conducting a more systematic investigation of this question.

A special category is represented by those functions of the organism which are regulated primarily by humoral means. After decortication of the cerebral hemispheres these functions change in a very different, one might even say opposite, manner compared to that of the reflex reactions and functions of the organism. The humoral agents evoke stronger and more protracted reactions in decorticated dogs than in normal animals. This is at least true of certain humoral substances and functions of the organism which we have investigated.

I. K. Zhmakin (1954) has demonstrated that the removal of the cerebral cortex in dogs does not to any appreciable degree affect the level of their basal metabolism. The slight decline in the level of basal metabolism which is observed after decortication may be regarded as the result of the decrease in the total brain mass, which is characterized by an extremely high metabolic rate. At the same time cerebral decortication causes a considerable intensification of the stimulating effect of moderate doses of adrenaline and thyroxine as well as of the act of eating on the metabolic processes of the tissues of the organism. The oxygen consumption by decorticated dogs under the influence of these factors is from 2 to 5 times that observed in the same dogs before decortication. Figure 8 illustrates the stimulating influence of moderate doses of adrenaline and thyroxine and of the intake of food. It must be pointed out that the considerably heightened sen-

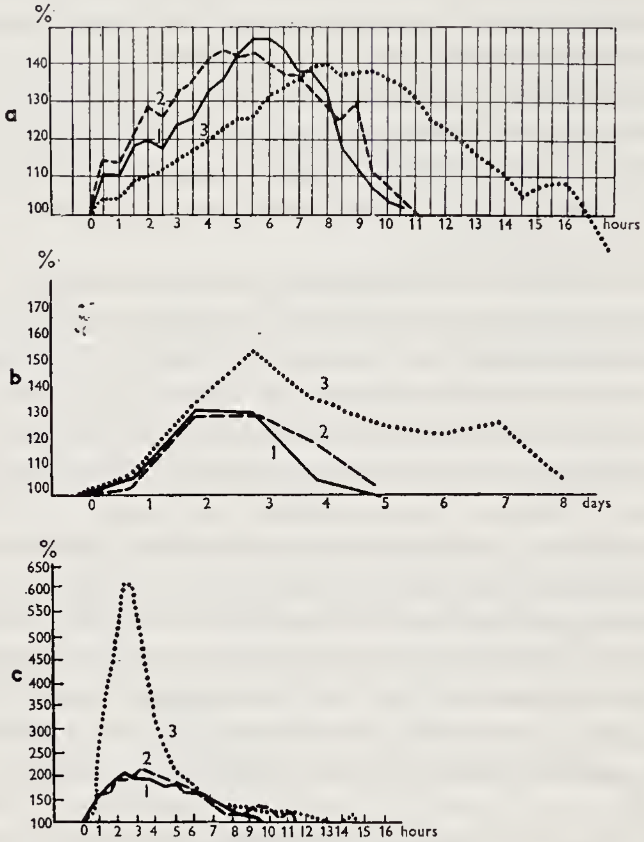

FIG. 8. Changes in the amount of oxygen consumption after taking food (a), introduction of thyroxine (b), administration of adrenaline (c). 1, in normal animal; 2, after unilateral decortication; 3, after total decortication.

sitivity of decorticated dogs to adrenaline and thyroxine is also reflected in changes which take place in the respiration, pulse rate, salivation and general condition of the animal. One of our decorticated experimental dogs died of severe adrenaline shock as the result of the injection of adrenaline in amounts which in normal animals (and even in unilaterally decorticated dogs) cause only insignificant changes in the respiration, pulse rate, and general condition of the animals.

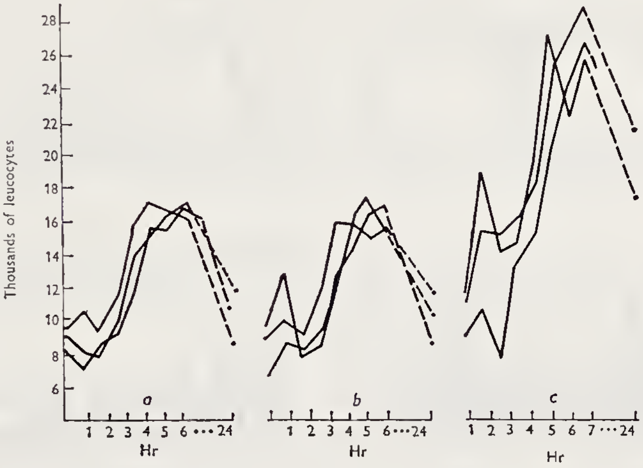

FIG. 9. Diagram showing the leukocytic reaction caused by the introduction of the sodium salt of nucleic acid in three normal dogs (a); after unilateral decortication (b); after total decortication (c).

I. P. Gur'eva and V. F. Marchenkov obtained preliminary data showing that the removal of the cerebral cortex also results in a considerable intensification of the hyperglycemic reaction to moderate doses of adrenaline and of the hypoglycemic reaction to moderate doses of insulin.

Our collaborators obtained some other similar data. According to the data of S. A. Chesnokova (1956), the injection of moderate doses of sodium nucleate evokes a stronger and more protracted leucocytosis in decorticated dogs than in normal dogs or in those which have been unilaterally decorticated (Fig. 9). Furthermore, A. V. Gubar' and F. A. Oreshuk (1956) demonstrated that moderate doses of a preparation of dry bile administered orally causes a considerably more pronounced intensification of bile secretion in decorticated dogs than in normal or unilaterally decorticated dogs. Of special interest are the data concerning the stimulation of the salivary and gastric glands in decorticated dogs by means of humoral agents. Zhmakin and Mal'tseva (1957) stimulated the secretion of the symmetric parotid salivary glands in unilaterally decorticated dogs either by giving food or by the injection of moderate doses of pilocarpine.

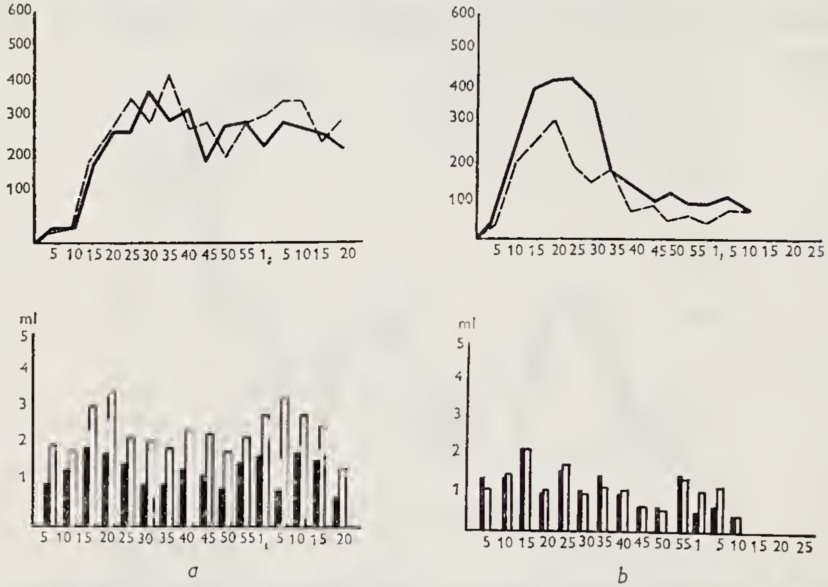

FIG. 10. Bars: the amount of saliva secreted by the parotid salivary glands of a dog after left unilateral decortication, after feeding with 30 g of dried bread (a), and after injection of pilocarpine (b); the black bars indicate secretion of the left gland, and the clear bars secretion of the right gland. Line graphs: concentration of radioactive sodium in the saliva; the ordinates show impulses per min in 1 ml saliva; the solid line indicates the left gland, and the dotted line the right gland.

They estimated the secretory activity of these glands both from the amount of saliva secreted and from the concentration of radioactive sodium. They made the following observations: while under the influence of reflex alimentary stimulation, the secretion of the affected salivary gland is a third to a half that of the control gland; during stimulation by pilocarpine it overtakes the control gland, so to speak, and secretes as much saliva as the latter. Even more significant is the observation that during pilocarpine stimulation the affected salivary gland secretes almost twice as much radioactive sodium as the control gland (Fig. 10). According to the data of

Markova, in decorticated dogs the so-called humoral phase of secretion of gastric juice during normal feeding is more intense and prolonged than in normal dogs, which is contrary to the phenomenon of reflex secretion of gastric juice during sham feeding. The secretion of gastric juice under such humorally acting stimulants as histamine, carbocholine and a dilute solution of alcohol also becomes greatly intensified (Fig. 11).

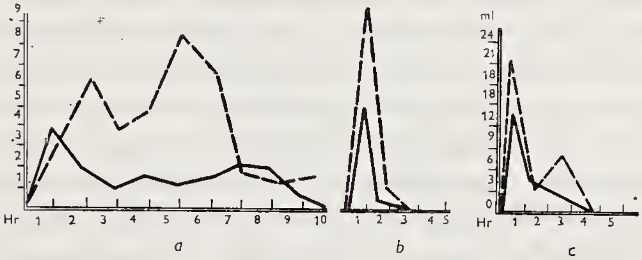

FIG. 11. The amount and dynamics of the secretion of gastric juice during feeding (a), after the injection of histamine (b), after the injection of a dilute solution of alcohol (c). — before decortication; – – – after decortication.

Of particular interest are the results of a series of experiments carried out in our laboratory by Vasil'eva and Kulikova, which seem paradoxical if we compare them with our other data. They fit neither into the framework of the first group of findings described above, nor into the framework of the second group; superficially they even appear to be in contradiction to both of these groups. To be more specific, Vasil'eva studied the influence of cerebral decortication in dogs on the development of anaphylactic shock. These experiments showed that unilaterally decorticated dogs differ very little from normal dogs with regard to the dynamics of development of sensitization to horse serum (subcutaneous injections of the serum at the rate of 0·1 ml/kg of body weight for 3 days), and with regard to the dynamics and intensity of development of anaphylactic shock under the action of the same antigen (intravenous injections of the serum at the rate of 0·02–0·1 ml/kg of body weight). Complete decortication of the cerebral hemispheres substantially changes the picture, markedly decreasing the reactivity of the organism to the antigen. Regardless of whether the dogs become sensitized before or after the removal of the cortex of the second hemisphere, anaphylactic shock either does not appear or emerges in a very weak form after the administration of such doses of antigen as usually evoke very profound anaphylactic shock in normal or in unilaterally decorticated dogs.

This phenomenon appears to contradict the previously described observations which show that the reactions to humoral factors become more intense after complete decortication, and is in somewhat closer agreement with observations which indicate a certain weakening of the reflex reactions under such conditions. One possible explanation of this phenomenon is as follows: although in this case we are dealing with the action of a humoral factor (a heterologous serum) on the organism, nevertheless the reactions evoked by it in the organism in the form of sensitization and anaphylactic shock are caused by a reflex mechanism. In other words, the humoral factor here chiefly plays the role of a stimulator of interoceptive reflexes.

We are inclined to interpret similarly the results of other experiments performed on dogs and rabbits by V. S. Kulikova. She investigated the effect of insulin on the content of sugar, inorganic phosphorus and leucocytes in the blood of intact and decorticated dogs and rabbits. A curious picture was revealed: the threshold dose of insulin required for a perceptible reduction of sugar and inorganic phosphorus in the blood is four to five times higher in decorticated dogs than in intact animals. While in intact animals it is approximately 0·06–0·07 units per kg. of body weight, in decorticated animals the dose is 0·30–0·35 units per kg of body weight.

Exactly the same phenomenon is observed in regard to the hyperglycemic reaction to the injection of adrenalin. In decorticated animals the threshold dose of adrenalin is two to three times that observed in normal dogs.

It seems to us that such a marked weakening of the glycemic reactions to adrenalin and insulin in decorticated animals can be satisfactorily understood if we assume that the mechanism of these glycemic reactions is essentially of a reflex nature. As is known, such a proposition has a solid experimental foundation in the light of modern physiology. It is enough to mention some reliable data indicating the presence of a specific glycemic reaction in the nervous structures of the hypothalamic area, as well as the important role played by the carotid receptors in the reflex regulation of blood sugar. The decline in the level of perfection of these reflex reactions and of their biological value as a result of cerebral decortication also appears in another peculiarity of the glycemic reactions in decorticated animals, namely, in the fact that the threshold doses of adrenalin and insulin approach very closely the maximum doses tolerated by these animals or, to be more precise, the doses which evoke profound and highly dangerous changes in the vital functions of the organism, particularly in the circulation and respiration. Thus, while in intact animals the dangerous dose of insulin is 10–12 times the threshold dose, in decorticated animals the dangerous dose is practically the same as the threshold dose.

The significance of these data concerning adrenalin and insulin is determined by one more circumstance. These experiments reveal not only the role of adrenalin and insulin as active humoral stimulants of certain reflex reactions of vital importance, but also their direct effect on the tissue processes in the organism, and on the functions of a number of organs and systems. This duality in the nature of the action of insulin on the functions of the organism is expressed, for example, in the fact that after cerebral decortication the sensitivity of the hypoglycemic reaction and of the reaction of a lowered level of inorganic phosphorus sharply decreases, while the sensitivity of the leucemic reaction not only does not show any decrease, but even increases slightly. With regard to the nature of the effect of adrenalin on the functioning of the organism, this duality manifests itself in the fact that the sensitivity of the hyperglycemic reaction decreases considerably after cerebral decortication, while the sensitivity of the general tissue reactions, especially the mechanisms which determine the development of shock-like states in the organism, greatly increases. Because of this, decorticated animals go into a very serious condition (which often ends in their death) as a result of doses of adrenalin which evoke only slight changes in the level of their blood sugar, while in intact animals these doses have practically no effect on the general condition of the organism, even though they evoke a stronger and more protracted hyperglycemic reaction.

Thus, some of the investigated effects caused by insulin and adrenalin in the organism before and after cerebral decortication are in accord with the above-mentioned somatic and vegetative reflex reactions, while other effects caused by the administration of insulin and adrenalin in these animals have much in common with the reactions of the tissues and organs to the direct action of humoral agents which have also been described above.

Along with the study of the functional changes which take place in the organism after cerebral decortication, we have started also to investigate changes which might occur in the structures of different organs and systems. Thus far we have only preliminary data of this kind which were obtained by F. A. Brazovskaia and which indicate that cerebral decortication in adult dogs evokes marked changes in the microstructure of a number of endocrine glands, namely degenerative changes in the adrenals and the hypophysis, and atrophic phenomena in the ovaries. As can be seen in the microphotographs, most of the follicles in the thyroid gland are distended (Fig. 12b), the walls of the follicles are markedly thinned, the epithelial cells are flattened, and most of the nuclei are pyknotic. The interfollicular connective tissue fibres between the distended follicles are absent. The colloid is unevenly stained. In a number of follicles the colloid is deeply stained and contains no vacuoles. In the ovaries (Fig. 13) the cortex is considerably deteriorated by primordial follicles. Occasional maturing follicles are in a collapsed condition, being overgrown with connective tissue (atresia) (Fig. 13b). Mature forms are absent. A considerable growth of connective tissue is observed in both the cortical and the medullary matter. The anterior lobe of the hypophysis reveals a diffuse, slight decrease in the number of cells, predominantly eosinophils. Some of the eosinophils are in a degenerated state (pyknosis of nuclei). In the posterior lobe of the hypophysis the number of cells is appreciably reduced, the cells themselves being smaller in size (Fig. 14b).

It must be pointed out that B. I. Baiandurov *et al.* (1949) in the course of their experiments resorted not to cerebral decortication as we did, but to decerebration; moreover, they performed this operation not on adult dogs but on puppies, after which they investigated the changes which took place in the growth of the puppies, in the trophic functions and structure of their various organs, etc. In spite of this essential difference between the character and direction of our experiments and those of Baiandurov *et al.*, there is some similarity between our data and theirs. This is particularly true in regard to the above-mentioned changes in the sensitivity of the operated animals to certain hormones.

Findings indicating the great importance of the cerebral cortex for the complete and precise unconditioned reflex activity of the central nervous system, as well as the results of our investigations of the

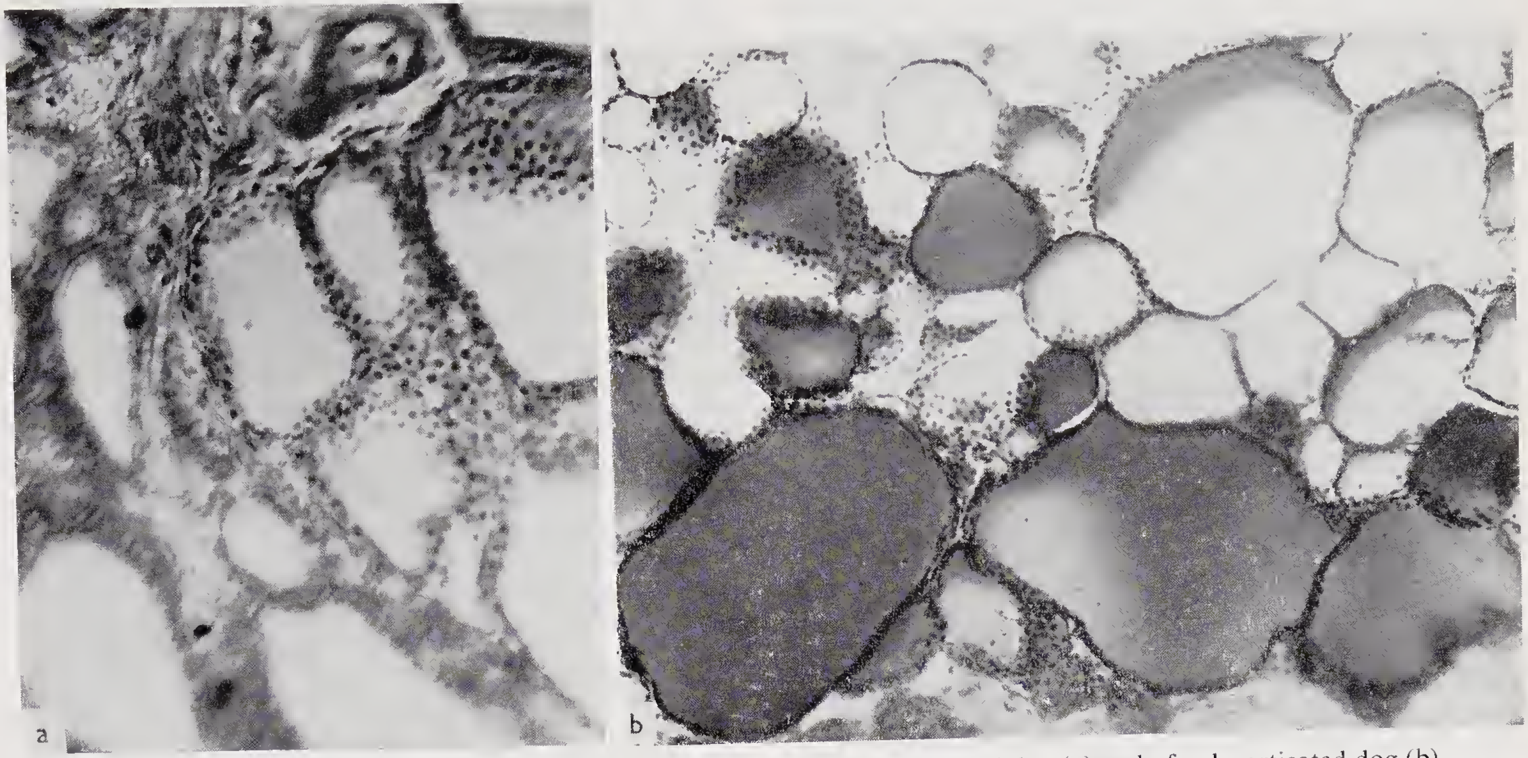

FIG. 12. Microphotograph of preparations of the thyroid gland of a normal dog (a) and of a decorticated dog (b).

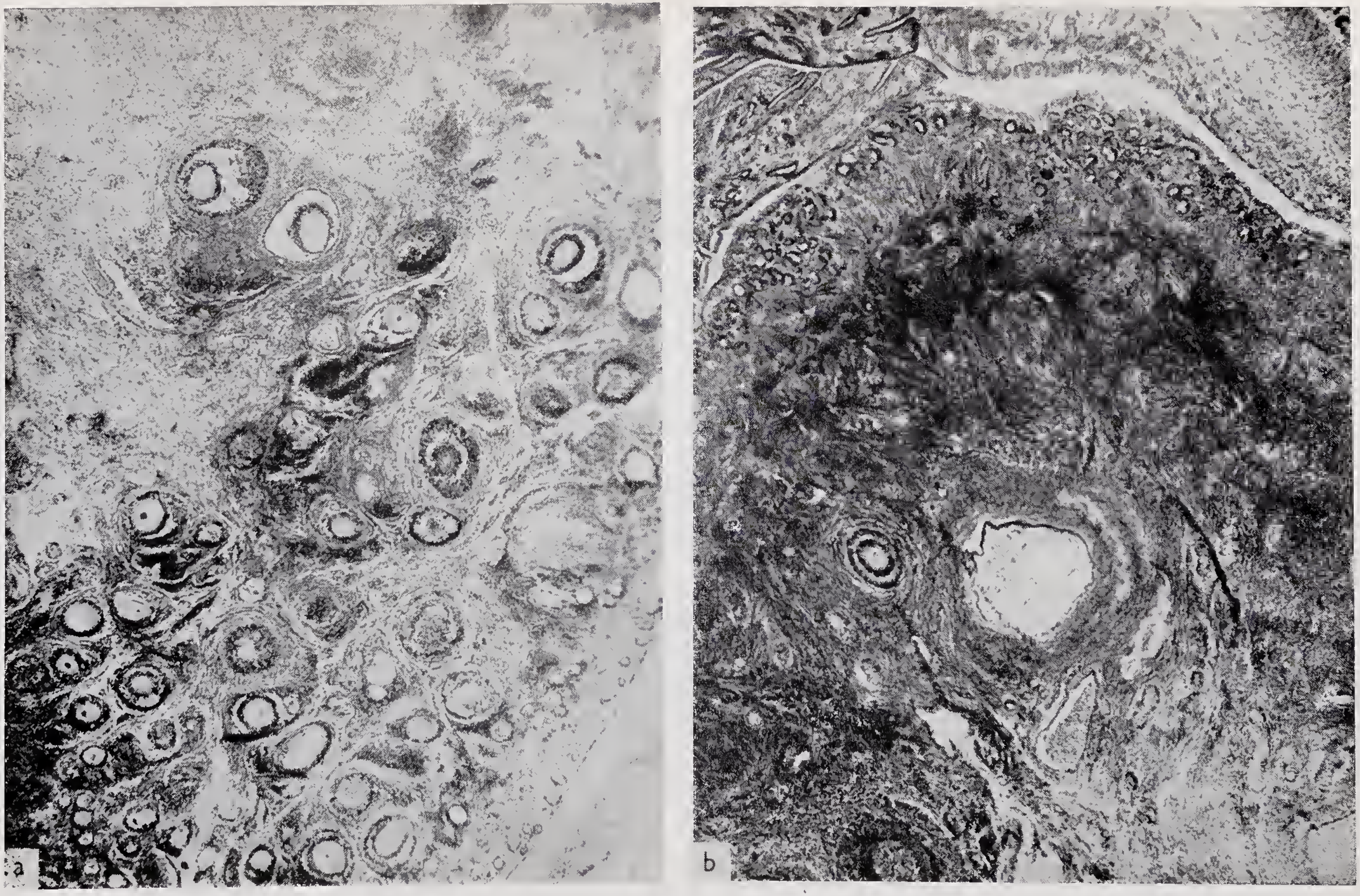

FIG. 13. Microphotograph of preparations of the ovary of a normal dog (a) and of a decorticated dog (b).

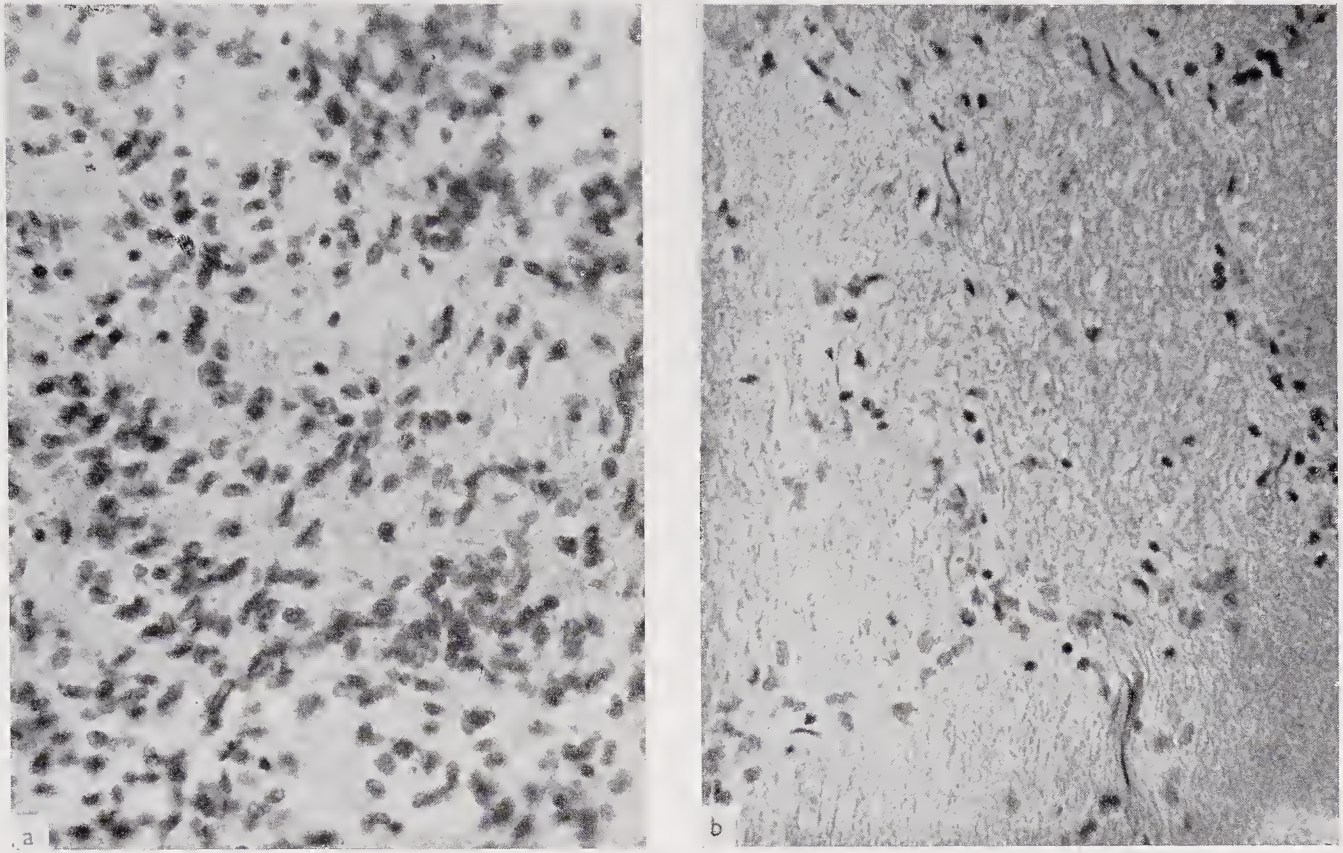

FIG. 14. Microphotograph of preparations of the posterior lobe of the hypophysis in a normal dog (a) and in a decorticated dog (b).

role of the cortex in compensating disturbed functions, investigations which we conducted for many years, led to the supposition that decorticated animals would prove highly vulnerable to various noxious influences.

As far back as the thirties, when we carried out experiments on a large number of decorticated dogs, we found obvious manifestations of a lowered resistance of the organisms to the action of pathogenic agents. Concomitant infections, sharp fluctuations of the external temperature, accidental errors in the feeding and care of the decorticated animals, were tolerated by them with great difficulty and in some cases led to their death. These general observations, made incidentally, have been confirmed by a special series of experiments performed in recent years.

We have stated above that the threshold sensitivity of decorticated dogs to the action of such humoral factors as adrenalin and insulin is considerably lower than that of intact animals. It is noteworthy that this reduced sensitivity is associated with a simultaneous decrease in the resistance of the animals to the action of doses which can lead to serious disturbances of certain vital functions. Whereas in the case of intact dogs the doses of adrenalin and insulin which can cause marked disturbances of respiration and cardiac activity are 10–12 times greater than the doses which can change the content of sugar, inorganic phosphorus and leucocytes in the blood, in the case of decorticated dogs these doses are almost the same. According to the data obtained by V. S. Kulikova, a slight change in the blood sugar of decorticated dogs occurs only as the result of an intravenous injection of 0·25 ml of 0·1 per cent solution of adrenalin, i.e. when the dose is 2·5 times the threshold dose for intact animals. An injection of this same threshold dose leads to a marked dyspnea, tachycardia and copious salivation, often followed by death. When this same dose of adrenalin is administered to dogs with intact brains, it evokes a marked and prolonged hyperglycemia and only very slight, transitory changes in respiration and in the cardiovascular system.

The results obtained in the administration of adrenalin fully accord with the data from our experiments with the injection of insulin. Judging by the changes which take place in the sugar and inorganic phosphorus content of the blood, the threshold dose of insulin for dogs with intact brains is 0·06–0·07 units per kg of body weight. In decorticated dogs similar changes are evoked only by a dose which is 4–5 times this amount, i.e. by a dose of 0·30–0·35 units. These, being threshold doses, at the same time proved to be bordering on the pathogenic for decorticated dogs. They evoked protracted hypoglycemia, which in the case of starved dogs often ended in death.

In this way, under the influence of decortication, the range of adaptability of the organism to the action of adrenalin and insulin becomes greatly reduced. This is the result of the disturbance of the nervous mechanisms regulating the blood sugar level which ensures biologically the very important combination of high sensitivity of the organism with its equally high resistance to changes taking place in the internal environment.

The data relating to the action of insulin and adrenalin have much in common with the results of the investigation of aseptic (turpentine) abscesses in decorticated rabbits and rats. The experiments performed by our collaborator S. A. Chesnokova showed that local inflammatory phenomena in the area of the injection of turpentine (the degree of oedema, the cellular composition of the exudate) are very slight in decorticated animals, but the general reaction of the organism to the local inflammation (loss of weight, temperature fluctuations, leucocytosis, etc.) is markedly intensified. A local injection of turpentine in decorticated animals was often accompanied by serious complications and in a number of cases led to their death. One can see that in the case of turpentine injections we again encounter a reduced reactivity of the decorticated animals, with a weak and sluggish local inflammatory reaction, along with a lowered resistance to the effect of the inflammatory process on the organism as a whole.

It was demonstrated that the laws governing the phenomena which manifested themselves in these experiments fully apply to the action of penetrating radiation. Our co-worker P. V. Simonov subjected to general X-ray irradiation decorticated and control rabbits, the skull of which had previously been trephined. He found that the higher part of the intact brain in rabbits is much more sensitive to the action of penetrating radiation than is the brain in decorticated animals. Thus a dose of 100 roentgens (which is comparatively low for rabbits) considerably reduces the duration of experimental catalepsy (animal hypnosis) in intact rabbits, while it does not have any effect on the duration of hypnosis in decorticated animals. However, the overall radiation resistance of the organism greatly diminishes under the influence of decortication. A dose of 400 roentgens is comparatively easily tolerated by intact rabbits and does not result in their death. The same dose in decorticated animals causes profound leucopenia, an early distortion of the leucocytic reactions during functional tests with the injection of sodium nucleate, and the death of 75 per cent of all the irradiated animals at the peak of radiation sickness, i.e. in the period between the ninth and seventeenth days. Decorticated rabbits exposed to irradiation during the state of subcortical neurosis (which we will consider later) tolerate the effect of irradiation with particular difficulty. These animals die on the fourth or fifth day after irradiation with a dose of 400 roentgens.

Until now we have been concerned with the resistance of decorticated animals to the action of pathogenic agents influencing highly diverse functions of the organism. We will now focus on the consequences of those noxious influences which are specifically aimed at the functional state of the higher parts of the central nervous system. We have in mind methods that are widely used in experimental practice in order to induce neurotic states in animals. As is known, the Pavlovian school considers disturbances of conditioned reflex activity as the basic symptom of experimental neurosis. To the degree that decorticated higher animals do not demonstrate any genuine conditioned reflexes, we can speak of their neurosis with some reservation, implying here only stable pathological changes of functional origin taking place in the activity of the subcortical formations of the brain.

Investigations carried out by our co-workers L. A. Miliutina and P. V. Simonov show that decorticated animals are much more susceptible to influences exerted on the functional state of the subcortical formations of the brain than animals whose cerebral cortex is intact.

Miliutina demonstrated that intact pigeons tolerate with comparative ease repeated stimulations of the leg by an electric current of threshold strength or slightly (1·5 times) stronger. Even 500 stimulations, at the rate of 12–14 per day in the course of 6–8 months, do not result in any essential changes in the general motor activity of pigeons, the birds do not lose weight and the females continue to lay eggs. The diurnal variations of motor activity in decerebrate pigeons becomes disturbed after 120–130 stimulations, and an almost continuous motor excitation appears. The body weight decreases, the functioning of the gastrointestinal tract becomes disturbed, and the feathers start falling out. This neurotic-like condition proves to be highly stable. Even interruptions of experiments for periods up to two months did not eliminate the motor excitation and did not improve the general condition of the birds. After 25–35 experiments (250–350 stimulations with electric current) the decerebrate pigeons usually died.

The results of the experiments of Miliutina agree with the data obtained by Simonov on rabbits. Simonov introduced 4–6 collisions of the defence and alimentary unconditioned reflexes in intact and decorticated rabbits by applying a painful stimulus by means of an electric current at the time of feeding. In control experiments the same stimulus was applied, but not at feeding time. Simonov demonstrated that this procedure did not disturb the general behavior and alimentary activity of intact rabbits and the resulting disturbances of certain vegetative functions disappeared in 25–40 days after the collision of the reflexes. In decorticated animals a collision of unconditioned reflexes leads to the appearance of a stable pathological condition of the subcortical formations of the brain which is characterized by the features of a defence dominant. The rabbits become excited, they rush about the cage and respond to the introduction of a syringe of food into the mouth with a strong defence reaction. The animals show an increasing loss of weight, loss of hair, disturbed activity of the gastrointestinal tract, and disturbance of some vegetative functions, particularly a distortion of the leucocytic reaction in response to the administration of sodium nucleate. As a rule these rabbits die 14–20 days later. Autopsy often shows that the mucous membrane of the stomach is eroded.

Simonov succeded in obtaining very interesting data concerning the role of the cerebral cortex in the compensation of functions disturbed as the result of an experimental neurosis. He had previously demonstrated that the removal of the cerebral cortex in rabbits which had undergone radiation sickness did not result in a repeated distortion of the leucocytic reactions. This is obviously due to the fact that radiation sickness affects the effector links of the given reaction, i.e. the blood-producing organs.

The situation is quite different in the case of experimental neurosis, where distortion of the leucocytic reactions is caused by the disturbance of the neuro-regulating mechanisms. Extirpation of the cerebral cortex in intact rabbits after full recovery of the functions disturbed as a result of neurosis, led in the experiments of Simonov to a repeated distortion of the leucocytic reactions in response to the injection of sodium nucleate. This phenomenon was not observed in control rabbits which had been subjected to stimulation by electric current without being fed simultaneously.

These are the basic findings relating to the resistance of the organism of decorticated animals to the action of noxious agents. What essential conclusions can be drawn from the experimental data obtained? We believe that we have no reason to regard the cerebral cortex as a division of the central nervous system which is particularly vulnerable to the action of absolutely all pathogenic agents. We have still less reason to consider the cortex as the "initiator" of pathological changes in the organism, or as the "organizer" of disturbances and distortions in the functions of the internal organs. It is true that the cerebral cortex is highly sensitive to any changes taking place in the external and internal environment of the organism. Under normal conditions this high sensitivity allows the cortex to effect the most precise and perfect regulation of the functions that are under its control. In pathological cases the cerebral cortex ensures the most expedient, rapid and flexible mobilization of all the defence forces of the organism, and of its numerous means of compensation. In all probability this function of the cortex is effected through its participation in defence and compensatory changes predominantly of a reflex type. It is easy to see that this supposition agrees well with the above-mentioned observations concerning the less perfect, functionally inferior unconditioned reflex activity of decorticated animals. If the nervous regulation of vitally important functions in decorticated animals proves imperfect even under normal conditions of their existence, one can imagine how fatal to the organism this inferiority may be under conditions of increased pathology. Moreover, it is possible that the cerebral cortex also exerts an influence on the humoral mechanisms of compensation through the nerve centres of the hypothalamus and the reticular formation of the brain stem.

Thus cerebral decortication in highly developed animals leads not only to a complete and irreversible disappearence of their higher nervous activity, but also to profound and persistent changes in their inborn reflex reactions, in the nervous and humoral regulation of the various functions of the organism, as well as in the structure of a number of organs, particularly of the endocrine glands.

Before proceeding to the explanation of the findings, we must mention one rather unfortunate circumstance. Both during our experimental work and in the course of the interpretation of its results, we could not avoid the difficulties which are characteristic of any investigations based on the application of partial, and especially of total, cerebral decortication and which have been experienced by many scientists since the time of Goltz. First, we have in mind the degenerative changes which inevitably take place in many nervous formations of the nearest subcortex, in the diencephalon, sometimes in the midbrain, and even in the lower parts of the central nervous system. These degenerative changes, which moreover vary in different experimental animals as to degree and extent, make it impossible for the investigator to claim categorical conclusions concerning the material substrate of the functions which disappear or are markedly changed after cerebral decortication. For this reason we cannot confidently exclude the possibility that the changes which we observed in the reflex reactions and functions of decorticated animals, are to some degree determined by degenerative changes occurring in those parts of the central nervous system which remain intact after the surgical operation. However, we can now definitely state that these changes in the reflex reactions and functions of the organism are for the most part definitely determined by cerebral decortication *per se*. This follows from the fact that, although with the lapse of time the degenerative changes in the intact parts of the central nervous system appear to become progressively more profound, the reflex reactions and functions of the organism, on the contrary, tend to become to some degree improved and perfected.

This is also corroborated by the following new data obtained in our laboratory by Mal'tseva. In dogs with chronic fistulae of the ducts of both parotid salivary glands, the cortex of one of the cerebral hemispheres was removed; this led to a marked and stable weakening of the reflex salivation of the ipsilateral salivary gland and a pronounced asymmetry in the secretory activity of the symmetric salivary glands. If after a period of more than one year after unilateral decortication the second hemisphere was also decorticated, the reflex salivation of both parotid salivary glands actually became equalized (Fig. 15).

If the degenerative changes in the subcortical structures played an essential role in the above described weakening of the reflex secretion of saliva, then, after the removal of the cortex of the second hemisphere, the reflex salivation of the ipsilateral salivary gland should for some time have greatly exceeded that of the symmetric salivary gland, and this should last until certain degenerative changes occurred in the subcortical formations of the subsequently decorticated hemisphere. Actually, however, this was never observed. The analysis of these data leads to the conclusion that degenerative changes occurring in the subcortical formations play an insignificant role, if any, in this repect.

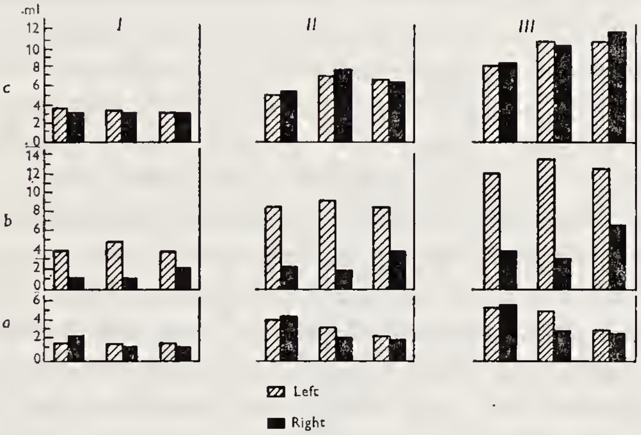

Fig. 15. Volume of reflex salivation of the parotid salivary glands of a dog in ml to 6 g (I), 12 g (II) and 15 g (III) of meat powder before decortication (a), after right unilateral decortication (b), and after subsequent left unilateral decortication (c). Each pair of bars indicates data from one experiment.

In this connection it must also be pointed out that, according to the data of Rioch (1940), cats deprived both of the cerebral cortex and of the basal subcortical ganglia, actually do not differ from cats in which only the cerebral cortex has been removed.

But even if we conclude that the changes caused by cerebral decortication in certain functions of the organism and in the structure of some of its organs, are to some degree determined by the subsequent degenerative changes in the subcortical nervous formations, this does not fundamentally affect the essence of the situation, since the changes which take place in the structure of the remaining subcortical formations are likewise caused by the cerebral decortication. Therefore in the final analysis we can reasonably regard all the changes which occur in the functions of the organism and in the structure of its peripheral organs after cerebral decortication as a direct or indirect result of this very decortication.

What, then, is our interpretation of the essence of the changes which occur in the unconditioned reflex reactions after cerebral decortication?

One of the possible theories is that such changes are exclusively or predominantly the result of the removal of the conditioned reflex component from the corresponding mixed or complex reflex reactions. However, this hypothesis seems to us improbable. It is hardly possible to ascribe to this factor any role in the changes which occur in such simple and complex reactions as adaptive reflexes following hemorrhage, or as reactions provoked by the injection of sodium nucleate, pilocarpine, Congo red, etc. It is hardly possible that one or two applications of such unusual stimuli, administered, moreover, at long intervals, should evoke corresponding conditioned reflexes. In the case of stimuli to which the experimental animals are accustomed, i.e. such stimuli as can undoubtedly also evoke natural conditioned reflexes (food, rejected substances, etc.), the role of this factor cannot be essential, because during the experiments these stimuli act upon the organism with no interval between them, i.e. their conditioned and unconditioned components act almost simultaneously. Under these circumstances unconditioned reflexes cannot be appreciably "complicated" by conditioned reflexes and therefore the removal of the conditioned reflex component from the complex reflex reaction could not cause any appreciable effects. In view of this, we interpret the above-described changes in the unconditioned reflex reactions and functions of the organism as the result of changes which take place in the neural apparatus underlying these reactions and which are caused by the removal of the cerebral cortex.

Moreover, we regard our findings concerning the changes which are caused in a number of reflex reactions and functions in a highly developed organism by cerebral decortication, as new and direct experimental corroboration of Pavlov's theoretical propositions concerning the structure and localization of specialized nerve centers, as well as the cortical representation of unconditioned reflexes. In the light of these theoretical propositions and on the basis of our data, we regard the cerebral cortex of highly developed animals not only as an organ of conditioned reflex activity, but also as an organ which participates in the accomplishment of unconditioned reflexes, i.e. as an organ of unconditioned reflex activity. According to these data the cerebral cortex, while participating in the accomplishment of unconditioned reflexes, intensifies them and makes then highly variable. dynamic, more complete and physiologically efficient. Apparently the participation of the cortex in the accomplishment of inborn forms of reflex activity is the more significant and complex the higher the organism is in the scale of phylogenetic and ontogenetic evolution. This participation reaches its greatest significance in regard to instincts in higher adult organs.

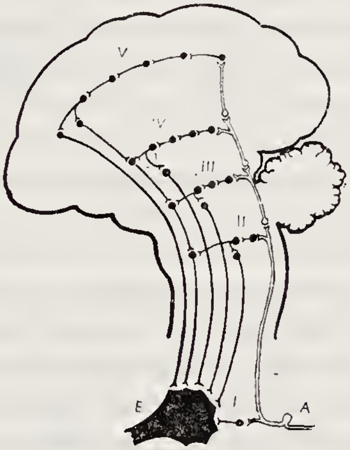

FIG. 16. Diagram illustrating the arc of the unconditioned reflex: I—V = branches of the central part of the reflex arc at different levels of the central nervous system; A, afferent neuron, E, efferent neuron.

We have been guided by the above theoretical propositions of Pavlov and have availed ourselves of the classical investigations of Sherrington and Magnus as well as of data of modern neurophysiologists concerning the characteristics of the integrative activity of different levels of the central nervous system, the functional subordination of its organs, and the corticalization of the organism's functions. We are thus able, on the basis of the findings here described and of a number of other data which we have obtained, to propose a new interpretation of the structure of the unconditioned reflex and a corresponding new schematic representation of its arc (Fig. 16).

According to our concept, the central part of the arc of an unconditioned reflex is not a single line; it passes not through a single level of the central nervous system, as is usually assumed, but consists of many branches, each passing through the main parts of the central nervous system: the spinal cord, medulla oblongata, midbrain, etc. The top branch of the arc passes through the cerebral cortex and is the cortical representation of a given unconditioned reflex, constituting the corticalization of the corresponding function of the organism.

This is not, however, a matter of reflex arcs of different lengths which have a common receptive field but different internuncial and efferent links and different effector organs, and which pass through different levels of the central nervous system, as might appear at first sight; rather, we are here dealing with different internuncial branches of *the same reflex arc* which pass through the above-mentioned levels and have the same receptive field and *the same efferent link and effector organ.* Judging by the available data, each of these branches has specific functional properties; by its participation in the accomplishment of an unconditioned reflex it imparts to this reflex a definite functional character and a definite level of perfection. It must be assumed that the special significance of each of these branches is different, not only for a given unconditioned reflex in organisms at various levels of phylogenetic and ontogenetic development, but for all the unconditioned reflexes of a given organism, varying according to the kind, type, complexity and other characteristics of these reflexes.

Moreover, although the entire intricate architecture of the arc of a given unconditioned reflex is believed to be fully activated during the stimulation of the corresponding receptive field, the degree of activity of each individual branch of the arc and its specific participation in the accomplishment of the reflex are not static and equal under all conditions. On the contrary, we suggest that there is great variability in this respect, depending on current local changes as well as on changes taking place in the functional condition and activity of the central nervous system as a whole. Finally, reflex arcs may possibly not contain branches which pass through certain levels of the central nervous system.

Obviously this scheme could be varied and complicated in various directions, taking into account the specific characteristics of the reflexes (Fig. 17). It is possible, for example, to indicate on the scheme the intermediate and efferent elements of the arcs of simultaneous vegetative reflexes (Fig. 17B), or to draw a scheme of the circular interaction between separate branches of the arc according to the closed circles type suggested by Lorente de No (Fig. 17 A).

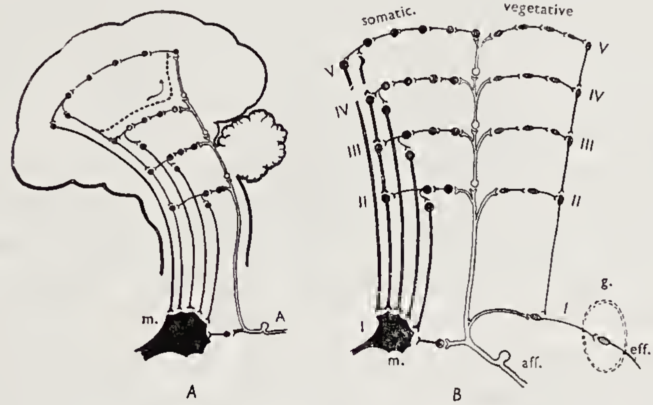

FIG. 17. Variations of diagram illustrating the arc of the unconditioned reflex.

We regard cerebral decortication as a destruction of the upper branch of this arc which results on the one hand in weakening, simplification and imperfection of the reflexes and of the reflex regulation of the functions of the organism, and, on the other hand, in increased sensitivity of the lower nervous and other structures of the organism to humoral agents, just as it occurs in the peripheral structures after transection of the nerves and spinal cord (Cannon and Rosenblueth, 1949, and others). Regarding decortication as a special "denervation" of the entire central nervous system, we are inclined to interpret this increased sensitivity to humoral agents in the light of the data and theoretical propositions of L. A. Orbeli (1942), namely, as the result of a certain retrograde functional readjustment of the "denervated" central nervous formations and peripheral organs and tissues, as a sort of return to the previously passed evolutionary stages which are characterized by a greater importance of the humoral factors in the regulation of the condition and functions of these structures.

Obviously the above proposition concerning the structure of the unconditioned reflex and the architecture of its arc is so far only a working hypothesis; but it seems to us that this hypothesis more than any other theoretical scheme permits us to unify and explain our findings as well as many other related findings of modern neurophysiology. It is impossible here to support this proposition even briefly in all its details, i.e. as regards all the branches of the reflex arc with its many levels, and to utilize for this purpose all available neurophysiological and neurohistological findings and concepts. We should, however, like to refer to some data obtained by other scientists as well as to some new arguments, in order to reinforce our experimental and theoretical support of that part of our hypothesis which directly concerns the present subject, namely, the participation of the cortex in the accomplishment of unconditioned reflexes and the role of the cortical branches of the arcs of these reflexes.

First, there are some reliable early and recent experimental data which indicate the existence of a cortical branch for every unconditioned reflex and which show that this branch, just like the basic, spinal branch of the reflex arc, is in a state of reflex tonic excitation; this excitation forms a functional background for the phasic activity of the cortical branch and exerts a constant, intensifying influence on the lower nerve structures. Specifically, we have in mind the following observations. At an early date Sherrington (1906), on the basis of reliable data, proposed the theory that the phenomenon of spinal shock in the caudal part of a transected spinal cord is caused by the interruption of the flow of facilitating and intensifying cerebral impulses to the nerve cells of this part. Later Fulton *et al.* (1946) developed Sherrington's original theory concerning the genesis of spinal shock and demonstrated that the cerebral cortex is one of the sources of these beneficial cerebral impulses and that in this respect the specific role of the cortex is greater the higher the evolutionary level of the given organism.

This line of research was continued by Adrian and Moruzzi (1939) who demonstrated in a series of experiments that the pyramidal tracts exhibit constant electric activity which, as regards its dynamics, is synchronous with the electric activity of the motor areas of the cortex, not only when the animal is in a state of wakefulness, but also when it is in narcotic sleep. If these cortico-spinal impulses are of moderate intensity, they cannot activate the motoneurons, but if the flow of these impulses reflexly increases, the motoneurons come into action.

Moreover, a number of histological, physiological and clinical findings show that in highly developed organisms there is a direct nervous connection not only between heterogeneous nervous elements of the same zone, but also between the nervous elements of different cortical receptor and effector zones. The presence of such intracortical local connections between heterogeneous nerve cells of different cortical layers is convincingly demonstrated, for example, by the classical cyto-architectonic investigations of Ramon y Cajal (1900—1906), Lorente de No (1934), and many others, as well as by the results of the recent meticulous physiological experiments of Burns (1950, 1951). He demonstrated that an isolated cortical slice with intact blood circulation can, in response to stimulation, show rhythmic electric activity which persists for some time after the stimulation has ceased, due to the circulation of the impulses along the closed circuits of the cortical nerve cells.

As to the presence of long nerve connections between different points of the cortex, this can be demonstrated (besides being supported by earlier data) by the results of the comparatively recent thorough histological investigations of Milch (1932), and by the physiological experiments of de Barenne, Carol and McCulloch (1941), and of McCulloch (1947). Milch extirpated small areas of the cerebral cortex in monkeys and studied the process of degeneration of the nerve fibres which extend from these cortical areas to others; he demonstrated the presence of numerous direct connections between the 6, 4, 3, 1, 2, 5, and 7 cortical zones according to Brodman. Dusser de Barenne and his co-workers, in the course of acute experiments on cats and monkeys, stimulated separate areas of the cortex by applying strychnine or electric current and then recorded the effect of these stimulations on the pattern of electric activity of other cortical areas; they thus demonstrated the presence of similar connections between a still wider range of cortical zones.

Nervous connections are here implied between the cellular elements of various cortical areas which are either close to or at a distance from each other. In the light of the theory of Luciani and Pavlov concerning the dynamic specialization and localization of functions in the cerebral cortex, these can be regarded as connections between the central or nuclear elements of corresponding projection zones. The existence of such nerve connections seems quite possible between the central elements of each projection zone and those peripheral elements of other zones which are near them, i.e. actually within their own zones.

These and other related observations provide adequate reason to regard and schematically to present the relationships between the nervous elements of a single cortical area, as well as between those of different cortical areas, as inborn connections, subject to laws, between the afferent, internuncial and efferent nerve cells of the cortical part of the reflex arc, as is the case with regard to the nerve cells of the spinal cord, medulla oblongata, etc. It should be pointed out that Lorente de No (cited by Fulton, 1946), Fulton (1955) and some other scientists held a similar view on this matter.

Modern neurophysiology has even more abundant data of a different kind, the analysis of which also leads to the conclusion that this concept and diagrammatic representation of the connections between the nervous elements of the cortical receptor and effector projection zones, as well as between the different elements of the same zone, is in considerably closer accord with demonstrated phenomena than are the prevailing concepts and schemes concerning the character of the relationship between these structures.

We have in mind the rich and varied experimental data of modern neurophysiology regarding the cortical representation of the receptor and effector systems of the organisms in even their smallest details; this material was largely obtained by means of the highly precise and elegant methods of microelectrophysiology. Unfortunately I cannot here give a complete review of these outstanding and exquisite investigations which delight all who value the progress of neurophysiology. I must therefore mention only some sample investigations of this kind and describe them in general outline. This will permit us to use them as criteria of the validity of certain hypotheses and concepts now current in neurophysiology concerning the principles which underlie the functioning of individual cortical zones and of the cortex as a whole; they will also help us better to evaluate the reliability of our above-stated hypotheses.

Recent years have brought radical changes to our previous understanding of the projection of various receptor systems in the cerebral cortex in higher animals and man, an understanding which was based on the results of early laboratory experiments involving the extirpation of separate zones of the cortex in animals, performed by Goltz, Ferrier, Luciani, Pavlov, and others, and on the clinical observations of Cushing, Foerster, Penfield and others, which were accumulated during brain surgery on a number of patients.

We may mention, for example, the demonstration in contemporary neurophysiology of the existence of duplicate somato-sensory, visual and auditory projection zones in the cortex of each hemisphere, the decription of the general and specific functional characteristics of each of these zones, the development of a highly precise and detailed scheme showing the localization in the corresponding zones of the representations of the peripheral elements which enter these systems, the demonstration of the "point to point" connections between these zones of the cerebral cortex on the one hand and the corresponding cerebellar zones on the other, etc.

We owe these remarkable achievements chiefly to Adrian, Bard, Woolsey, Bremer, Mountcastle, Bailey, Marshall, Fulton, Dell, Amassian, and their collaborators, who demonstrated and skillfully utilized the possibility of generating so-called evoked potentials in the functional units of the cerebral cortex during natural or artificial stimulations of the elements of the external and internal receptors, of central nervous organs or tracts, and of separate nerve roots or branches containing afferent fibres.

Appreciable success has also recently been attained in the study of the motor function of the cerebral cortex; these new data substantially enhance and deepen our former understanding of this question, which was based on the early laboratory investigations of Goltz, Horsley, Schäffer, Sherrington, Pavlov, Vogt, and others, as well as on the clinical observations of Jackson, Krause, Cushing, Foerster, and others. New investigations in this field are also being carried out largely by means of modern, highly perfected electrophysiological methods which are often combined with electrical or strychnine stimulation of separate areas of the cortex, antidromal stimulation of the afferent nerve cells of the cortex, and surgical injury of certain cortical zones, subcortical formations, descending nerve pathways, etc. These investigations, performed by Penfield, Woolsey, Ward, Chang, Fulton, Tower, Kennard, Hines, Dusser de Barrenne, McCulloch and others, demonstrate a number of important observations such as the existence of basic and complementary cortical motor zones, the existence in the cortex of special areas which exert a strong inhibitory action on motor activity, the high variability of motor effects caused by the stimulation of the same points of the motor zones, etc.

In order to avoid digression from the main significance of the findings which we are now discussing, we shall not even briefly consider them here from all possible points of view. We shall only point out in passing that the definite limits of the cortical projection zones, which were demonstrated in the course of these investigations, probably include only the central or "nuclear" part of these zones according to Pavlov. Indeed, such investigations carried out largely by means of acute experiments in which many factors may greatly alter the functional state of the cerebral cortex, can hardly reveal the peripheral or dispersed elements of these zones even by means of the finest stimulating or recording microelectrodes.

How does modern neurophysiology interpret, theoretically elucidate and generalize all these findings and data from the point of view which we are here considering?

It is no exaggeration to state that in this respect the state of affairs is far from satisfactory, and that there is obvious discord between the experimental and theoretical studies of the abovementioned problems as well as of others concerning the physiology of the cerebral cortex. The present state of affairs is characterized by a considerable divergence of views and opinions concerning the interpretation, understanding and appraisal of the data from the point of view of the localization of functions in the cortex and the relationship between the cortical localization zones; it is also characterized by the absence of any generally accepted basic theoretical propositions, at least with respect to such fundamental questions concerning the activity of the cerebral cortex as are closely connected with this problem. Regarding the sensory and motor functions of the cortex as the beginning and end of its activity, and proceeding from the observation that under conditions of artificial stimulation of the cortical motor and sensory projection zones it is possible to reproduce only elementary discrete movements and sensations, different investigators approach differently the general principles of these zones and of the cortex as a whole.

As stated above, modern neurology has numerous data which indicate the existance of afferent and efferent nerve elements and their interconnection within each cortical receptor and effector projection zone, and the existence of direct nerve connections between the nervous elements of different cortical zones. Nevertheless, the traditional concept still persists, especially the schematic representation of the receptor and effector cortical projection zones as cortical areas which consist of functionally homogeneous elements with no organized and definite nervous pathways between them, i.e. entirely separate from each other. At the same time it is assumed that these zones can communicate functionally with each other either diffusely, i.e. not in definite directions, through the medium of certain specific cortical zones which dominate them, or through extra-cortical nerve centers and formations of a higher order.

For example, many scientists still hold the old concept of the presence of association areas in the cortex which possess specific structural and functional features, and, in particular, can form and unify the activity of the projection zones and effect almost unaided such higher cerebral functions as learning. memory, speech, etc. (see, for example, Fulton, 1955). However, not only according to the physiological data of Luciani (1915), Pavlov *et al.*, Lilly, Hughes and Galkin (1956), and other investigators, but also according to the morphological data of Freeman and Watts (1950), Glees (1944), Walker (1938), and others, the so-called association areas of the cerebral cortex do not differ essentially from its projection zones and are similarly connected with the subcortical formations.

In this case the investigators underestimate the role of the nervous elements of the projection zones in the achievement of higher integrative activity, since they reason from data which have been obtained under highly abnormal conditions for the functioning of these elements, especially for their higher integrative activity (anesthesia, trephination of the skull, exposure of the brain, artificial stimulation, etc.). In other cases, on the basis of the same data (which are in no way significant in this respect) they belittle the role and significance of the cerebral cortex as a whole. For example, there is a point of view according to which the cerebral cortex lacks higher integrative properties in general, and is subordinated in its activity to other nervous formations (the centroencephalic system, the reticular formation), which are located in the area of the diencephalon and play a leading role in the achievement of the higher integrative activity of the brain (Penfield, 1954; Jasper, 1954; Fessard, 1954, and others). Some scientists assert the existence of a certain undetermined principle which controls the activity of the cerebral cortex (Eccles, 1953).

It would be deplorable, of course, if in the approach to this question, just as to any complex scientific problem, there were complete uniformity of views and opinions. This would deprive science of one of the most powerful stimuli for its development. However, the progress of any branch of science requires generalizations, common denominators which make possible the comparison and juxtaposition of homogeneous and even heterogeneous data, general principles which cover a potentially wide range of phenomena. Figuratively speaking, a kind of general architectural design is needed which would allow us to arrange into a certain system and in a proper order various building materials in order to obtain a complete and harmonious structure. Even a superficial comparison of the experimental and theoretical research work which is being conducted in two related spheres of modern neurophysiology will make it possible to show graphically the great importance of such a guiding general principle, of such a general architectural design.

We believe that the extremely valuable and varied new data concerning the physiology of the spinal cord which Eccles, Renshaw, Lloyd, Lorente de No, Woodbury, Paton, Barron, Araki, Fuortes, Hunt, Sprague, Ström, Kostiuk, Motsni and others are obtaining by means of modern microelectrophysiologic and some other methods of investigation, are more thoroughly understood and more generally applied than the above-mentioned data concerning the function of the cerebral cortex which modern investigators are obtaining by means of similar perfected methods of research and which are no less valuable and varied. A definite role in this respect is of course played by the great complexity of the functions of the cortex and by its far more extensive and complicated connections with other organs of the central nervous system. It seems to us, however, that the following circumstance here also plays an essential role. The above-mentioned investigators of the functions of the spinal cord are always guided in their experimental and theoretical work by the principle of reflex activity. They skillfully arrange the varoius data obtained in the course of refined experiments according to the appropriate structural elements of the architecture of the reflex, i.e. they invariably follow the path which was indicated by the classic investigations of Sherrington on the physiology of the spinal cord.

However, the great majority of scientists engaged in the investigation of the functions of the cerebral cortex show a quite different attitude towards the reflex principle as a general basis of the activity of the organ under investigation. Some consider it inapplicable to the cortex; others do not formally reject it but nevertheless do not take it into account and disregard or underestimate it. Under these circumstances one can understand the persistent nature of fractional concepts as to the separate and fragmentary representation of elements which enter the peripheral receptor and effector systems of the organism in the corresponding projection zones of the cortex, as to their homogeneity and the absence of any connection between them, as to the limited and subordinate role of the cortex as a whole in the integrative activity which is usually ascribed to these zones, etc. This is the situation in the absence of any other commonly accepted and guiding general theoretical principle and of any other general architectural design. This in spite of the fact that as long as one hundred years ago Huxley (1868) in Britain, Sechenov (1866) in Russia, Groesinger (1844) in Germany and other advanced thinkers of that time announced their bold and progressive concept of the reflex origin and nature of cerebral activity; subsequently in his classic investigations Pavlov developed the concept of conditioned reflex activity as related to the physiology of the cortex of the cerebral hemispheres.

In studying experimentally and theoretically the question of cortical representation of the receptor and affector systems of the organism, many modern neurophysiologists underestimate not only these truly epoch-making events in the development of the physiology of the brain and the findings and concepts of Luciani and Pavlov concerning the dynamic specialization and localization of functions in the cortex, but also another profound concept which was advanced by Pavlov in the last period of his creative activity and which opened up bright prospects for the investigation of this very question. We refer to the concept of the cortical representation of unconditioned reflexes. We ourselves were guided by this idea in our above-mentioned investigations which led to its formulation, i.e. our proposition concerning the participation of the cortex in the accomplishment of unconditioned reflexes and the existence of a special cortical branch of the arcs of these reflexes which form the structural basis of this participation. However, although many investigators underestimate the reflex principle and are guided not by Pavlov's idea but by other ideas and concepts, it seems to us that their data concerning the cortical representation of the receptor and effector systems of the organism can be satisfactorily understood, interpreted and more fully unified and generalized strictly on the basis of the *reflex principle* and in the light of this idea of Pavlov.

The concept of the cortical representation of the components of different receptor and effector systems of the organism, which is generally accepted among the above-named neurophysiologists, is by no means identical with the concept of the cortical representation of unconditioned reflexes, as some physiologists believe; it is not based on the idea of reflex, but only expresses the idea of fragmentary and purely afferent or purely efferent points of the cortex and not that of a naturally connected chain of heterogeneous nerve elements in the form of the central part of a reflex arc. This also relates to a considerable extent to the concept of so-called cortical centers of various somatic and vegetative functions of individual organs. We believe, however, that these concepts can be harmonized and that any step in this direction and even towards their complete fusion is fully justified. This can be achieved by postulating that the cortical projection zones contain not only afferent or only efferent elements, but both, with the possible predominance of these or other elements in different zones, as well as by postulating that between the heterogeneous components of each projection zone there exist organized nervous connections like those between the links of the central part of the reflex arc. As we have seen, there are more morphological and functional reasons and logical arguments for these concepts, and even for the concept that there are similar connections between the components of different cortical projection zones, than for the hypothesis that these projection zones play a passive, non-creative role in cerebral activity and are strictly subordinate to certain dominant cortical or extracortical zones, centers or principles.

The great principle of the reflex activity of the nervous system which was advanced more than three hundred years ago by Descartes and which was brought to its present high level of perfection and significance by Sechenov, Sherrington and Pavlov, undoubtedly is among those creations of the human mind which have stood the test of time.

We believe that the time has come for modern neurophysiology to apply more completely to the entire nervous system the idea of the universality of the principle of reflex activity and widely to recognize the reflex as the fundamental principle of activity of the central nervous system, including its higher parts. This is undoubtedly the most reliable and effective way of overcoming the existing confusion in the approach of different scientists to the theory of the functions of the cerebral cortex; it would also serve as a powerful stimulus for further and still more fruitful experimental and theoretical work in this field.

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CHAPTER 4

THE PHYSIOLOGY OF THE CONDITIONED REFLEX

THANKS to the basic investigations of Sechenov (1886), Pflüger (1853) Sherrington (1906), Pavlov (1897), Magnus (1924), and others, the modern reflex theory regards the inborn reflex not as a homogeneous and stereotyped form of activity of the nervous system as was previously assumed, but as a dynamic, changeable and mobile form. It is well known at present that even the simplest inborn reflexes in the most primitive animals may vary greatly in intensity, duration and nature, depending on the condition of the reflex apparatus and of its separate links, on the kind and strength of the stimulus and the duration of its action, and on a number of other internal and external factors. As these reflexes become more and more complex in the course of evolution, so also do their dynamics and lability steadily increase. It is not difficult to understand the biological significance of this lability of the inborn reflexes and of its evolution. Indeed, the central nervous system, being a peculiar "physiological skeleton" of all the functions of the organism, plays the role of the chief agent and regulator of its adaptive activity by means of the reflexes, including those that are inborn. Hence it is clear that the variability of the reflexes raises their adaptive potential, and that the variability itself by its very essence has an adaptive character.

But if the phenomenon of lability is a characteristic and biologically important feature of inborn reflexes the role of which consists mainly in integrating the internal life of the organism with its relatively stable internal factors, what then are the level and significance of the lability of conditioned reflexes which are the chief regulators of the "external life" of the organism, which ensure its finest and most perfect adaptation to the external environment with its continually changing factors, and which constitute the essence of individual adaptation?

Pavlov regarded the conditioned reflex as the central physiological phenomenon in the activity of the cerebral hemispheres. According to Pavlov, a high degree of lability, its temporary and dynamic nature and dependence on specific conditions are the chief and most characteristic properties of the conditioned reflex. Pavlov (1949) wrote: "It is lability that characterizes the nervous phenomena under investigation: every moment and under every condition they take on a new trend" (p. 144). It is obvious that lability, like all the other basic characteristics, is not uniformly manifested in the conditioned reflex. Although the conditioned reflex, which is the basis of individual adaptation, "exists throughout the entire animal kingdom," as stated by Pavlov, this reflex did not remain unchanged. In the process of evolution it rapidly developed, as a result of which there appeared a great variety of conditioned reflexes, different in their character, type, manifestation, degree of complexity, level of development, degree of lability and other characteristics.

Thus, the lability of unconditioned and particularly of conditioned reflexes is marked by the diversity of their forms of manifestation and of the factors by which they are determined. A particularly important type of lability of reflexes is that which is determined by a preliminary change in the condition of the central system of these reflexes resulting from special afferent nerve impulses, which are caused by initial bodily position or by some other stimuli, i.e. by essentially reflex pathways.

This type of lability of reflexes was first revealed approximately one hundred years ago by Sechenov in the reflex activity of the spinal cord; it was subsequently investigated by Sanders-Ezn (1867), Goltz (1869), Sherrington (1900), and especially by Magnus on vertebrates, and by Uexküll (1909) and Jordan (1915) on invertebrates. For greater clarity, I shall refer to the first and highly illustrative experiments of Sechenov on spinal frogs. These experiments demonstrated that the inital position of the limbs often predetermines the character of the reflex to be expected from the stimulation of a certain receptive field. For example, if the hind limb which is to be subjected to stimulation is initially flexed, the stimulation of the digits evokes its extension. On the other hand, if it is initially extended, the same stimulation of the same receptive field calls forth the opposite reflex and the limb is flexed. The analysis of this phenomenon led Sechenov to the conclusion that the initial position of the limb exerts an influence on the functional condition of the spinal reflex apparatus through the corresponding proprioceptive and exteroceptive afferent systems. That is to say, depending on the position of the limb, different intracentral relationships are created between the components of this apparatus, thereby determining the character of the future reflex reaction.

Similar results were obtained by all the other above-mentioned investigators. They based their interpretations of this phenomenon mainly on the same point of view as did Sechenov. Magnus, who thoroughly investigated this type of lability of spinal reflexes in dogs and as thoroughly analysed it experimentally, designated it as "switching" (schaltung). It is under this name that this phenomen has entered modern neurophysiology.

Not long ago Ward (1950), in a series of experiments on cats and monkeys as well as in the course of observations on patients during brain operations, established a new variant of switching. He found that electric stimulation of a certain point in the motor zone of the cerebral cortex, corresponding to a definite limb, evokes one or another type of movement in that limb, depending on its initial position. Moreover, in a series of experiments on animals, Ward demonstrated that this phenomenon disappears after the deafferentation of the limb. Thus he established that in this case, just as in the above-described variant of switching, the lability of the motor reaction is determined by the influence of the flow of nerve impulses which originate in the receptors of the limb and reflect its initial position.

In conditioned reflex activity this type of lability was not subjected to special study for a long time, although individual investigators occasionally made certain observations which suggested its existence. But even aside from these occasional and sporadic observations, there were sufficient theoretical grounds for such an assumption. We have in mind the important proposition of evolutionary physiology that the laws governing the activity of the various organs of the central nervous system, no matter how specific they are, have common biological roots and many common traits, and that in the activity of these organs, along with particular and specific features, there is a common element which develops according to "a single plan" although at different levels, or, figuratively speaking, along different turns of an ascending spiral. If the phenomenon of switching as a particular form of lability of reflexes was demonstrated in the activity of the primitive central organs, there was reason to believe that this phenomenon, while exhibiting some specific features, was also inherent in the higher central organs the reflex activity of which, as stated above, is characterized by marked lability.

During the past 20 years our laboratory (Asratian, 1938, 1941, 1954, 1957) has been engaged in special and systematic experimental investigations of the phenomenon of switching in conditioned reflex activity, as a specific form of its lability. Almost simultaneously a number of other scientists, Konorskii and Miller (1936), Laptev (1938) and others, started investigations in the same direction. At present this subject is already attracting the attention of numerous scientists who are engaged in the study of the physiology of higher nervous activity.

I shall turn now to a concise statement of the basic concrete data obtained by us and our collaborators, as well as of our theoretical propositions based on these data.

Drawing an analogy with switching in unconditioned reflex activity, we set ourselves the task of demonstrating experimentally the possibility of elaborating two different conditioned reflex responses to the same stimulus, which could thus evoke one or another conditioned reflex depending on the initial state of the reflex apparatus. The problem, therefore, consisted in simultaneously giving two different signal meanings to a single conditioned stimulus.*

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* The material contained in the rest of this book will be more clearly understood if the reader will keep in mind the fact that the author discusses three types of conditioned reflex experiments:

1. Switching *(perekliuchenie* in Russian), sometimes redundantly translated as "trans-switching." In these experiments the same neutral stimulus (CS) is reinforced with a different unconditioned stimulus (US) in different situations, e.g. with food in one chamber and with electric shock in another chamber; or different US are used as reinforcement at different times of day or by different experimenters. The same neutral stimulus thus acquires the property of provoking a different conditioned reflex (CR) under different circumstances.

2. Dual or binary conditioned reflexes *(dvoinye* or *binarnye* in Russian). A dual CR is developed by reinforcing the same CS *simultaneously with two different US* (e.g. food and electric shock to a paw), so that the animal eventually gives a dual response to the same CS (e.g. simultaneously lifting the paw and salivating).

3. Bidirectional conditioned connection *(dvustoronniaia uslovnaia sviaz'* in Russian). The author states that when a conditioned reflex is being developed, two connections really take place:

It should be pointed out that, in the course of studying the so-called heterogeneous conditioned reflexes, Pavlov's laboratories long ago obtained a number of data which show that the usual signal meaning of a conditioned stimulus can be changed quickly and temporarily to another meaning. If, for example, in experiments with heterogeneous conditioned reflexes some stimuli are alimentary signals while others are electric defence signals, it is possible by means of preliminary intensification of the excitability of the food center (for example, by starving the experimental animal) to make the electric defence conditioned stimuli evoke an alimentary reaction. An opposite effect can be obtained by first decreasing the alimentary excitability or by intensifying the excitability of the defence center. A temporary change of the signal meanings of the conditioned stimuli can also be effected in another way. If soon after the feeding of the animal, i.e. when its food center is still in a state of excitation, we apply an electric defence conditioned stimulus, this evokes an alimentary conditioned reflex, and not one of electric defence. Similarly, an alimentary conditioned stimulus which follows residual excitation of the defence center evokes an electric defence conditioned reflex (according to the data of Konradi, 1932, and Konorskii and Miller).

This type of rapid and transitory modification of the signal meaning of a stimulus is somewhat similar as to physiological mechanism to the phenomenon which manifested itself especially strongly in the well known experiments of M. N. Erofeeva (1912), and which vividly demonstrated the significance of the relative excitability of various unconditioned reflex centers in determining the character of condi-

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(a) a direct CR where the CS evokes the CR;

(b) a reverse CR where the application of the US alone provokes a response corresponding to the CS, e.g. when a mild electric shock to the paw (CS) is reinforced with food (US), eventually application of electric shock will induce conditioned salivation (a direct CR). When food is presented (US) to the animal it will provoke a lifting of the paw, i.e. a conditioned motor defense reflex (a reverse CR).

The Russian phrase *dvustoronniaia uslovnaia sviaz'* literally means a bilateral conditioned connection. The word "bilateral" has a specific anatomic connotation, implying responses by two symmetric organs or extremities. This anatomic connotation, however, is not involved in these experiments and is therefore confusing. For this reason we have used the word "bidirectional." — S.A.C.

tioned reflex activity. In all these cases, the laws governing the inborn forms of activity of the central nervous system, result in switching nerve impulses from some pathways to others, thus causing one reflex or another. It is precisely this phenomenon which Pavlov (1949) had in mind when he spoke of the "switching of the nervous current," and when he stated that "on reaching the higher part of the nervous system the stimulus is transmitted now in one direction and now in another, depending on the given conditions" (p. 207).

In all these experiments the modification of the signal meaning of the conditioned stimulus was not specially elaborated, but occurred because of an accidental predominance of the excitability of one unconditioned reflex center over another, i.e. it was the result of the laws governing inborn nervous activity. The mechanism of these phenomena has much in common with the mechanism of the phenomena of reversal, dominant, etc., which were demonstrated by some investigators during direct or reflex stimulations of the cortex under acute experimental conditions. We have in mind, for example, the experiments of Graham Brown and Sherrington (1912) in which it was established that if, after stimulation of the cortical point which leads to the flexion of one of the limbs we stimulate the cortical point usually causing its extension, we will then obtain flexion of the limb in this case also, instead of extension. Experiments of a similar sort by Ukhtomskii (1927) demonstrated that if, for example, after a reflex excitation of the swallowing center we stimulate the cortical point of an extremity, this will not result in a movement of that extremity, but in a swallowing movement.

In our laboratory we tried to solve a somewhat different problem: to carry out a special elaboration of two stable conditioned reflexes to the same stimulus, i.e. establishing two different and constant signal meanings for the same stimulus. Such a switching would not be subject to the laws of the inborn forms of nervous activity, but to those of the acquired forms of this activity.

Our experimental procedure was essentially as follows. In its initial stage our collaborator F. M. Shitov (1937) performed the following experiments on dogs: in the morning, by pairing metronome tones of 120 beats per min with food, he converted those tones into a positive alimentary conditioned stimulus; he differentiated from them metronome tones of 60 beats per min by not reinforcing with food, i.e. he converted the latter into a negative conditioned stimulus. After these reflexes had been stabilized another investigator, V. V. Iakovleva, conducted different experiments in the same chamber on the same dogs and on the same day, but some hours later. She systematically paired the metronome tones of 120 beats per min with stimulating the dog's paw by electric current. Several days later the dogs developed an *electric defence* reflex to this stimulus during experiments conducted in the afternoons, while in the mornings the metronome tones of 120 beats per min acted as a positive *alimentary* conditioned stimulus.

The following observation is quite interesting. After the electric defence reflex to 120 beats per min had been formed and reinforced in afternoon experiments, the differentiation to 60 beats per min of the metronome was immediately evident during the very first application. Subsequently a number of other stimuli were turned into alimentary conditioned stimuli by the first experimenter in morning experiments and into electric defence conditioned stimuli by the second experimenter during afternoon experiments.

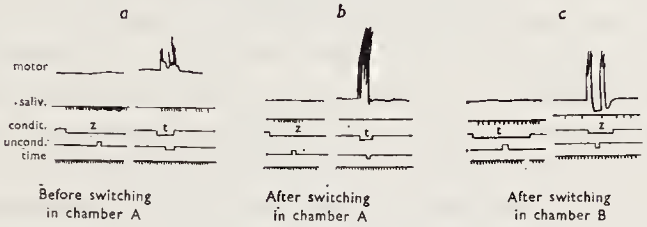
These experiments thus made it possible to give the same stimulus two different positive signal meanings so that it evoked a conditioned reflex of one kind or another, depending on the circumstances.

Special experiments demonstrated that the investigators themselves were the agents of switching the conditioned reflexes in the above-described cases. When the experiments were conducted by Shitov the stimuli had an alimentary signal meaning, irrespective of the time of day and the sequence of the experiments, while the same stimuli in the experiments conducted by Iakovleva had an electric defence signal meaning. Moreover, when during control experiments the devices used for alimentary conditioned reflexes or electric defence conditioned reflexes were attached to various parts of the animal's body, the results of the experiments were not noticeably affected. When, however, both Shitov and Iakovleva were present at the experiments, the result was considerable confusion in conditioned reflex activity, i.e. the dogs reacted to the stimuli sometimes as to a food signal, sometimes as to an electric defence signal, and sometimes their reactions were mixed.

We established through other experiments that numerous other factors might be the switching agents of conditioned reflexes, such as changing the chamber, alterations in the equipment of the chamber. changes in the time or sequence of the experiments, etc. For instance, if both experiments on the same dog are conducted by the same investigator in the same chamber but at different times of day and in a definite, unvarying sequence, it is possible to turn the same stimulus into an alimentary conditioned signal in one series of experiments and into an electric defence conditioned signal in another series of experiments. The results will be similar if the same investigator conducts each of the experiments in a separate chamber; in that case the time of day and sequence of experiments is of no essential importance. These and other factors can each become separate switching agents, but their combination facilitates this complicated transformation in the activity of the cerebral hemispheres and can prevent possible disturbances.

It has been demonstrated in our laboratory that animals can solve even more complicated problems connected with the switching of different conditioned reflexes. M. I. Struchkov (1956) formed two different conditioned reflexes in dogs in the same chamber, i.e. an alimentary conditioned reflex to the sound of a buzzer and an electric defence reflex to a tactile skin stimulus. After these conditioned reflexes had become well stabilized, Struchkov began parallel experiments on the same dogs in different chambers, this time pairing the tactile skin stimulus with food and the buzzer with electric stimulation of the paw. The experiments conducted in the second chamber had considerable influence on the conditioned reflex activity of the dogs when they were placed in the first chamber. The important point, however, is that the dogs finally solved the difficult and complicated problem in a rather clear-cut and precise way, after overcoming the resultant neurotic state, and after passing through the phase of double conditioned reflex action to each of the stimuli and the phase of gradual increase of adequate reaction and decrease of inadequate reaction to each stimulus in a given chamber (Fig. 1).

In a special series of experiments we also demonstrated that it is possible to form a positive and a negative conditioned reflex of the same kind to a single stimulus, i.e. that it is possible to switch conditioned reflexes from one functional sign to the opposite sign within the limits of a single type of activity of the organism, giving the same stimulus the ability either to activate or to inhibit a specific function (unpublished experiments by F. M. Shitov and V. A. Zamiatina). The very same investigator conducted two experiments on dogs in the same chamber: one in the morning and one in the afternoon. In both experiments only alimentary conditioned reflexes were formed and only to the same stimuli. The only difference between the two experiments was that in the morning experiment all conditioned stimuli, without exception, were reinforced by food, whereas in the afternoon experiment one of the stimuli was not reinforced by food. That particular stimulus acquired, as a result of the experiments, a double signal meaning: in the morning experiments, like all the other stimuli, it acted as a positive alimentary conditioned stimulus, while in the afternoon experiments, unlike the other stimuli, it acted as a negative conditioned stimulus, causing no reflex.



Before switching in chamber A
After switching in chamber A
After switching in chamber B

FIG. 1. Kymogram of conditioned reflexes in a dog. (a) before the elaboration of a switch in chamber A: a conditioned salivary alimentary reflex (in drops) to the sound of a buzzer (z) and a double conditioned reflex (electric defence and alimentary) to a tactile stimulus (t); (b) after the elaboration of a switch in the same chamber: a conditioned salivary alimentary reflex to the sound of a buzzer (z) and a conditioned electric defence motor reflex to a tactile stimulus (t); (c) after the elaboration of a switch in chamber B: a conditioned salivary alimentary reflex to a tactile stimulus (t) and a conditioned electric defence motor reflex to the sound of a buzzer (z).

We subsequently demonstrated that animals can also solve more complicated problems of switching conditioned reflexes of one kind but of opposite functional signs. In the morning experiments Shitov (1939) paired a loud tone with food, while a soft tone was not paired with food; he reversed the procedure in the afternoon experiments conducted in the same chamber and on the same dogs, pairing the soft tone with food while the loud tone was not paired with food. The aim was to give each of these two similar stimuli opposite signal meanings within the limits of one kind of conditioned reflex activity. The problem proved to be rather difficult and in these experiments it was not solved by all the dogs. Some of the dogs solved it, though not in a very well-defined manner. In the morning experiments the loud tone evoked the positive conditioned reflex and the soft tone either did not produce it at all or evoked it in a weak form. Conversely, in the afternoon experiments the soft tone evoked the positive alimentary conditioned reflex, while the loud tone produced it in a weak form.

The experiments of my colleague Ia. M. Pressman (1941) (somewhat similar to those of Iu. Konorskii and S. Miller) show that it is also possible to switch conditioned reflex activity, i.e. to change the signal meaning of the stimulus within the limits of one kind and one sign of conditioned reflexes. Pressman attached electrodes and a movement recording device to the right hind paw of a dog and by pairing various neutral stimuli with electric stimulation of that paw, produced corresponding motor electric defence conditioned reflexes. When the conditioned reflexes in the right paw were established, Pressman conducted another experiment: he attached the same electrodes and recording device, not to the right paw but to the left, which had never before been stimulated with electric current and in which no conditioned reflex had been developed. The very first time the conditioned signal was applied, the dog raised its left hind paw, i.e. the paw to which the electrodes and the recording equipment had been attached for the first time (Fig. 2). Obviously in this case, as in similar experiments by Konorskii, the switching of the conditioned reflexes from one paw to the other was caused by the act of attaching the recording devices and the electrodes to the paws. When in another experiment the electrodes and the devices were attached to both hind paws, the dogs became confused. The first time the conditioned stimulus was applied, the dog lifted and put down first one hind paw and then the other in turn. But after the very first electric stimulation of one of the paws, all subsequent reactions took place in that paw only.

Thus in the first series of Pressman's experiments the switching of the conditioned reflex activity was due to the act of attaching the electrodes and the recording device to the dog's paws, whereas in the second series of experiments this role was played by the first stimulation of the paw by electric current.

Until recently we and our co-workers and other scientists were investigating the kinds of elaborated switching in conditioned reflex activity in which, depending on conditions, the stimulus either signaled different activities, i.e. activated different functions of the organism, or gave two opposite signals in the same activity, i.e. activated one specific function. But the following question still remained unsolved: is it possible to elaborate a kind of conditioned reflex switching in which a single conditioned stimulus would call forth two conditioned reflexes of the same type (for example, two alimentary reflexes), and of the same functional sign (for example, positive), but of different magnitude and different latency, depending on specific conditions. In other words, is it possible within the limits of a signal meaning of one kind and of one sign to give to a single conditioned stimulus different properties, specifically, the ability to evoke either a weak or a strong positive conditioned reflex with a short or a long latency?

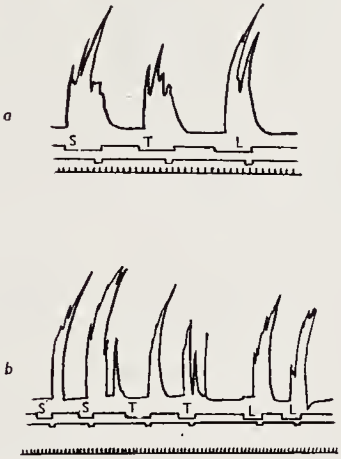


FIG. 2. Kymogram of electric defence conditioned reflexes to the sound of a bell (S), to a tactile stimulus (T), and to light (L) in dog "Jan". (a) in the right hind paw to which the electrodes and the recording device were previously attached and in which reflexes have been elaborated; (b) in the left hind paw, to which the electrodes and the recording device were attached for the first time. From top to bottom: reflexes; lines of the conditioned stimulations; line of the unconditioned stimulations; time in sec.

In this connection should be recalled the early observations of Pavlov's collaborators, and especially data yielded by the later researches of Kleshchov (1936), Nikitin (1933) and others, according to which the intensity of a conditioned reflex may be determined not only by the intensity of the conditioned stimulus, but also by that of the unconditioned reflex on the basis of which it was elaborated.

Specifically, the above-mentioned investigators established that by means of a substantial increase or decrease in the intensity of the unconditioned reinforcement and consequently in that of the unconditioned reflex, it is possible to obtain a considerable corresponding increase or decrease in the intensity of the conditioned reflex which was elaborated on the basis of this unconditioned reflex to the same stimulus, without changing the intensity of this stimulus. Further, the results of numerous investigations carried out in Pavlov's laboratories showed that by varying the delay of the reinforcement of the conditioned reflex to a certain stimulus it is possible to obtain a corresponding change in the latent period of this conditioned reflex, for example, to convert it from a short latency to a long latency reflex, and vice versa.

It is easy to see that these two kinds of experiments were aimed at the solution of problems which are quite different from those mentioned earlier. In both cases, i.e. in the experiments where the intensity of the conditioned reflex is modified by a corresponding change in the magnitude of the reinforcing unconditioned reflex, as well as in the experiments where the latent period of the conditioned reflex is modified by a corresponding change in the time of delay of the reinforcing unconditioned reflex, the conditioned stimulus at a given time has the ability to evoke only one of two possible conditioned reflexes: either strong or weak, with either a short latency or a long latency.

On the basis of these as well as other observations we could, of course, easily yield to making various conjectures and theories concerning the possibility of solving the above problems by higher animals, i.e. of elaborating those characteristics of the conditioned stimulus whereby, in accordance with these or other conditions, it could at a given moment evoke either a strong or a weak conditioned reflex, with either a short or a long latency. But no matter how justified and probable such conjectures may seem, they cannot replace precise laboratory experimentation in the solution of complex scientific problems, especially of such intricate problems of higher nervous activity as the possibility of giving to a single conditioned stimulus simultaneously two different signal meanings within the limits of one type of reflex and one functional sign. That is why we considered it necessary to concern ourselves with the direct experimental investigation of these still unsolved questions regarding the problem of elaborated switching in conditioned reflex activity. With this aim, appropriate experiments were carried out in our laboratory by two young Chinese physiologists, Zhu Zi-Jiao and Yan Wei-Jin.

The experiments of Yan Wei-Jin (1957) were as follows. In one chamber (I) she elaborated in dogs alimentary conditioned reflexes to acoustic, visual and tactile stimuli, reinforcing each of these stimuli with 20 g of powdered dried meat and bread. When the conditioned reflexes to all the stimuli reached adequate strength and stability in this chamber, the experimenter started new experiments in another chamber (II), the same stimuli this time being reinforced with 60 g of the same food. Finally, the experiments were performed in each chamber in turn, one day in the first chamber and one day in the second, the stimuli being reinforced with portions of 20 g and 60 g of food respectively. In order to ensure an approximately equal alimentary excitability, the experiments were carried out at the same hour in both chambers. In order to avoid the formation of a stereotype, the sequence of the stimuli and the intervals between their application were continually varied in both experiments. The conditioned stimuli were delayed for 15 sec in both cases.

Disregarding the variations observed in the results of the experiments which were determined by individual peculiarities of the experimental animals, as well as many interesting details which characterized the dynamics of the development of these phenomena, we shall dwell here only on the essentials common to all the experimental animals. The alimentary conditioned reflexes to all stimuli underwent a number of phasic changes in both chambers and finally reached a relatively stable strength which was, however, different for each chamber: in chamber II it was almost one and a half to two times as great as in chamber I; in chamber II the latent period of the conditioned reflex was shorter, while the intensity of the conditioned salivation was greater than in chamber I. The above can be illustrated by data which were recorded during the final stages of experiments carried out on two dogs in both chambers. In the dog "Likhe" in chamber I the visual signal for a period of 15 sec evoked a conditioned reflex equal in strength to 29 divisions of the scale, whereas in chamber II this conditioned reflex equalled 56·2 divisions. The action of a tone produced 25·5 divisions in chamber I and 63 in chamber II. In the dog "Solove' " the corresponding figures were: for the visual signal, 59 and 80 divisions; for the tactile stimulus, 56 and 81·2 divisions; and for the tone, 44 and 76 divisions (Fig. 3).

The experiments performed by Zhu Zi-Jiao (1957) on dogs were of a different kind. First, alimentary conditioned reflexes to auditory, visual and tactile stimuli were elaborated in one chamber by means of reinforcement of each of these stimuli with 60 g of powdered dried meat and bread. In order to demonstrate conditioned reflexes, the unconditioned stimuli alone were applied for 15 sec, after which the food was presented. When the conditioned reflexes reached adequate strength and stability in this chamber, the experimenter started new experiments in the second chamber; the difference between the experiments carried out in the first chamber and those in the second was that in the second chamber portions of food of the same amount and kind were presented to the animals, not 15 sec after the conditioned stimuli began to act, but after a delay of one or two minutes. From that time on the experiments were performed alternately in each chamber, the same stimuli being reinforced with the same amount of food, presented after a delay of 15 sec in the first chamber and after a delay of one to two minutes in the second chamber. The experiments took place at the same hour but, as in the previous experiments, the sequence of the stimuli and the intervals between them were constantly varied.

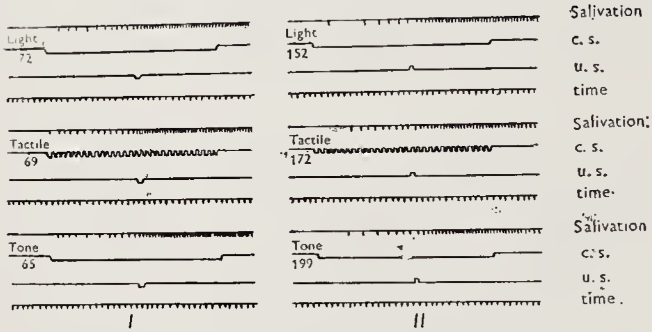


FIG. 3. Kymogram of salivary alimentary conditioned reflexes to light, to a tactile stimulus and to a tone elaborated in the chambers by means of reinforcement with large portions (I) and small portions (II) of food.

These experiments revealed certain individual peculiarities among the animals, but here we shall dwell neither on these peculiarities nor on the data which characterize the development of different phases in the solution of this problem. The most important result of the experiments is the following observation which was common to all the experimental animals: whereas in the first chamber all the conditioned stimuli evoked in the animals reflexes with a short latent period, in the second chamber they produced reflexes with much longer latent periods. The short latency conditioned reflexes were considerably weaker than those with long latency. For example, in comparable experiments of this stage the latent period of a conditioned reflex elaborated in the dog "Dadutz" to a tactile stimulation of the skin was 7 sec in the first chamber and 25 sec in the second chamber; the latent period of a conditioned reflex to the visual stimulus was 4 sec and 34 sec respectively, and to a tone 4 sec and 8 sec. In the dog "Tarzan" the corresponding latent periods of the conditioned reflexes were: to a tone 3 sec and 26 sec; to a tactile stimulation of the skin, 2 sec and 16 sec; to the visual stimulus, 2 sec and 32 sec. The diagram (Fig. 4) shows the dynamics of the elaboration of this variant of switching conditioned reflexes, or, to be more precise, the dynamics of modifications in the durations of the latent period of salivary conditioned reflexes as well as in their magnitude at the three basic stages.

It should be observed that the elaboration of variously delayed and variously reinforced alimentary conditioned reflexes to the same stimuli also proved possible when experimentation was conducted on the same animals in the same chamber and at the same time of day. but by different experimenters and on different days.

Of considerable interest are the following data obtained on dogs by Yan Wei-Jin and Zhu Zi-Jiao after their successful elaboration of differently delayed and differently reinforced conditioned alimentary reflexes . If at this stage of experimentation a conditioned reflex of a given delay (for example, a short latency reflex), or of a given amount of reinforcement (for example, the small reinforcement) has been elaborated to the new stimulus in one chamber, then the very first application of this stimulus in the other chamber produces a conditioned reflex with the delay characteristic of the second chamber (a long latency reflex), or of the corresponding amount of reinforcement (large reinforcement). In this case also the *tonic* conditioned reflex background (represented by the particular conditioning chamber. Ed.) determines the character of the *phasic* conditioned reflex (i.e. the conditioned reflex obtained in response to a specific conditioned stimulus. Ed.). Furthermore, if in one chamber we completely extinguish the conditioned reflex to a certain stimulus, the conditioned reflex to the same stimulus in the other chamber also becomes markedly inhibited. Obviously under our experimental conditions

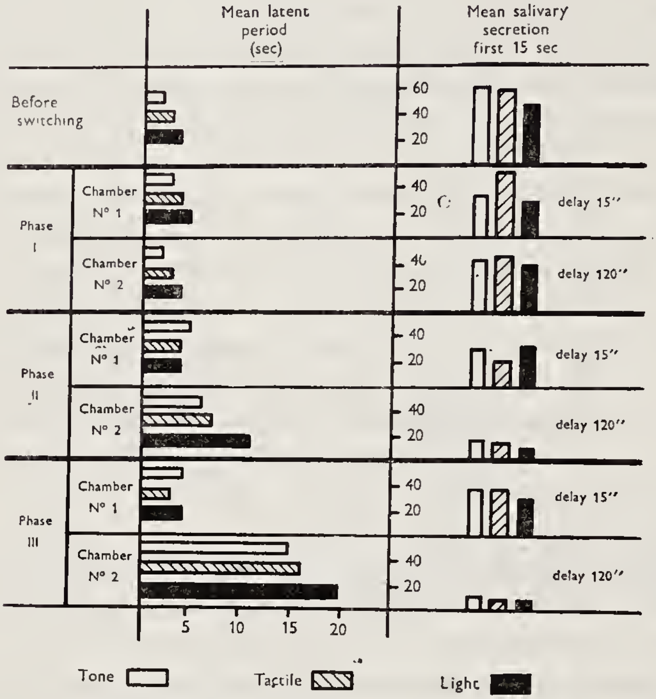


FIG. 4. Diagram showing changes in the average duration (in sec) of the latent periods (horizontal bars) and intensity (vertical bars) of salivary conditioned reflexes to a tone, a tactile stimulus and light in the course of elaborating a switch to the respective durations of their latent periods.

both of the differently *reinforced* conditioned alimentary reflexes to the same stimulus, as well as both of the differently *delayed* conditioned reflexes to the same stimulus, are effected by the same nervous structures.

Thus these experiments show that it is possible to elaborate in dogs the switching both of differently reinforced and of differently delayed positive alimentary conditioned reflexes to the same stimulus. It should be pointed out that the achievement of this result proved to be quite difficult for the experimental dogs. Some of them went into a state of neurosis even during elaboration of the switching, while others did so after its termination; this led sometimes to the disruption of the level of switching already attained, sometimes to the breakdown of the entire conditioned reflex activity, and even to changes in the external behavior of the dogs. Only a recess in the experimental work, and in some cases the administration of moderate doses bromide preparations, made it possible to overcome these difficulties and to normalize the disturbed higher nervous activity in the experimental animals.

What, then, is the physiological mechanism of the above-described phenomena, and what are our theoretical concepts in regard to switching in conditioned reflex activity?

We believe that the constant factors of the environment or of the experimental conditions which we designate as "switching agents" (different chambers, experimenters, hour of experimentation, sequence of the experiments, etc.) and which in the final analysis determine the signal meanings of ordinary conditioned stimuli of short duration, are in effect conditioned stimuli in themselves. But these stimuli, just like the conditioned reflexes which they evoke, are of a *specific type* and differ from ordinary conditioned stimuli and reflexes. The constantly acting factors of the environment or of the experimental conditions, which are at first neutral, gradually become *constantly acting conditioned stimuli* which can evoke *conditioned reflexes of a tonic type*, and create a definite functional background or readiness for phasic activity. These tonic conditioned reflexes can specifically adjust the phasic conditioned reflex pathways and mechanisms and thereby predetermine the type and functional sign or character of the phasic conditioned reflexes which emerge against this background, as well as the direction of the phasic conditioned reflex activity in general.

With regard to the elaborated switching of heterogeneous conditioned reflexes, for example, the above statements can be graphically illustrated by a diagram (Fig. 5) which shows the various cortical points of the stimuli and the connections between them. A conditioned stimulus (with cortical point S) in one of the chambers (I) is linked by a phasic conditioned connection (a) with an unconditioned alimentary reflex (with cortical point A) and evokes an alimentary conditioned reflex along the chain S—a—A. The same stimulus in the other chamber (II) is also linked by a phasic conditioned connection (b) with an electric defence unconditioned connection (B) and evokes a corresponding conditioned reflex along the chain S—b—B. The specific manifestation of one or the other of the heterogeneous signal meanings peculiar to this conditioned stimulus, is determined by the fact that corresponding tonic conditioned reflexes to the switching agents have simultaneously been elaborated, i.e. an alimentary reflex to chamber I and an electric defence reflex to chamber II. On the diagram the tonic conditioned reflexes are designated by arrows; I—A and II—B. This does not mean that the tonic conditioned reflex modification of the functional state which takes place in each chamber is in one case confined only to the cortical point of the alimentary unconditioned reflex, and in the other case to that of the electric defence reflex. There are definite reasons to assume that this conditioned reflex modification is accompanied by a change in the functional state of the corresponding *phasic* conditioned connections and even of the cortical points of the conditioned stimuli.

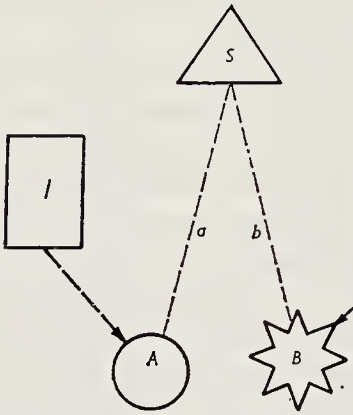


FIG. 5. Diagram showing the switching of heterogeneous conditioned reflexes.

It is probable that the changes in the functional state of these two structures are of a secondary nature and that they are determined by tonic conditioned reflex changes in the cortical points of the corresponding unconditioned reflexes, just as it takes place (according to the latest neurophysiological data) in the nervous structures of simple reflex arcs during the appearance in them of so-called local excitation and during the decrement of the latter by diffusion in all directions, including the antidromal. In this case the connection of the switching agents with the corresponding cortical points of the unconditioned reflexes can be designated, as in Fig. 5, by chains I—A—a—S and II—B—b—S. It is possible, however, that each of the switching agents is connected directly with each of these chief cortical links of the phasic conditioned reflexes, and can consequently modify their functional state directly, but simultaneously and in the same direction as the changes in the functional state of the cortical point of the unconditioned reflex. In this case, the schematic presentation of these interrelations has to be complicated, and the diagram must be changed by at least adding two arrows pointing from each switching agent to the corresponding phasic conditioned connections (I—a and II—b) and to the cortical point of the conditioned stimulus which is common to the phasic conditioned reflexes of both types (I—S and II—S).

We now have new data which may be regarded as direct experimental corroboration of our hypothesis to the effect that the phenomenon of switching represents a tonic conditioned reflex. Our coworker G. T. Sakhiulina (1955) investigated the phenomenon of switching in conditioned reflex activity in dogs by means of the usual methods of conditioned reflexes combined with electroencephalography. In experiments performed in the morning an auditory stimulus was paired with the electric stimulation of the dog's left hind leg, while in the afternoon experiments the same auditory stimulus was paired with the electric stimulation of the right hind leg. The experiments estabilished the possiblity of elaborating a switch in the dog's conditioned reflex activity (i.e. in the morning the auditory stimulus caused the dog to lift its left hind leg and in the afternoon its right hind leg). At the stage of distinct switching in the conditioned reflexes a new and interesting phenomenon in the EEG of the dogs was observed: as soon as the preparation of the animal for the experiment was begun (i.e. when it was brought to the chamber and placed on the stand, when the necessary instruments were attached to different parts of its body, etc.), there appeared a focus of heightened electric activity in the anterior parietal area of the cortex in the cerebral hemisphere homolateral to the activated leg. This focus of heightened electric activity persisted throughout the experiment. From the sections of the electroencephalograms of two such experiments shown in Fig. 6 it can be seen that during the morning experiments this focus emerges in the above-named area of the cortex of the left hemisphere while during the afternoon experiments it appears in that of the right hemisphere. An auditory, i.e. phasic, conditioned stimulus applied against this background, at the time of its action increases the degree of electric activity of other cortical points and simultaneously intensifies even more the electric activity of the particular point. It is noteworthy that topographically this point coincides quite closely with the cortical point which, according to Bremer (1953) and others, integrates the postural reflexes.

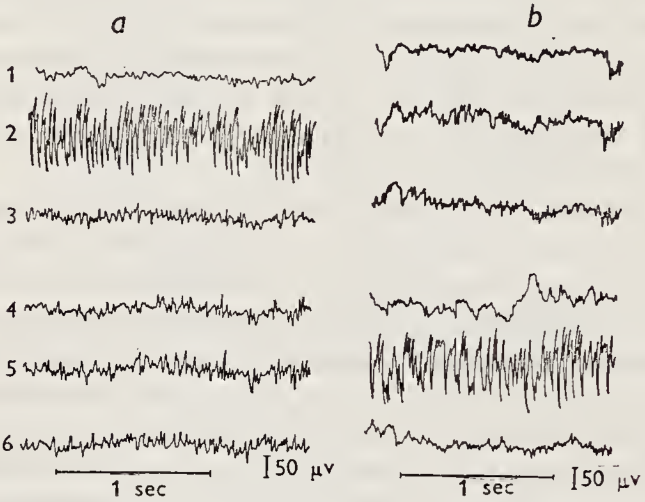


Fig. 6. Electroencephalogram of the dog "Tsygan" during a switch of electric defence motor conditioned reflexes from one extremity to another. (a) morning experiment; (b) afternoon experiment. 1, 2, 3, leads from the left cerebral hemisphere; 4, 5, 6, leads from the right cerebral hemisphere; 1, 4, frontal leads; 2, 5, leads from the boundary between the frontal and parietal areas; 3, 6, leads from the occipital areas.

Thus, the above experimental data regarding the nature of the electric activity of the cortex clearly show that two types of conditioned reflexes actually develop and appear during elaborated switching in conditioned reflex activity: *tonic conditioned reflexes* determined by the constant factors of the experimental conditions, and *phasic conditioned reflexes* which emerge against this background and which are evoked by the application of specific short-acting conditioned stimuli.

The following data obtained in our laboratory by Khachaturian also testify to the formation of tonic conditioned reflexes. We first determined as precisely as possible the salivary reflex produced in the dog by a standard portion of dried bread and meat (10 g) under the conditions of the experimental chamber. All the values obtained in this way were in general almost identical. Then, during a period of more than a week, in the same chamber the dog received considerably larger portions of the same food (50 g or more); this of course evoked a much stronger salivary reflex. After this series of experiments we resumed feeding the dog with the original size portions of dried bread and meat (10 g); this time the salivary reflex proved to be stronger than originally. Figure 7 shows the values of the salivary reflexes observed at the three stages of experimentation described above. It is noteworthy that after several days of feeding the dog for the second time with 10 g portions, the salivary reflex gradually diminished and returned to its initial value.

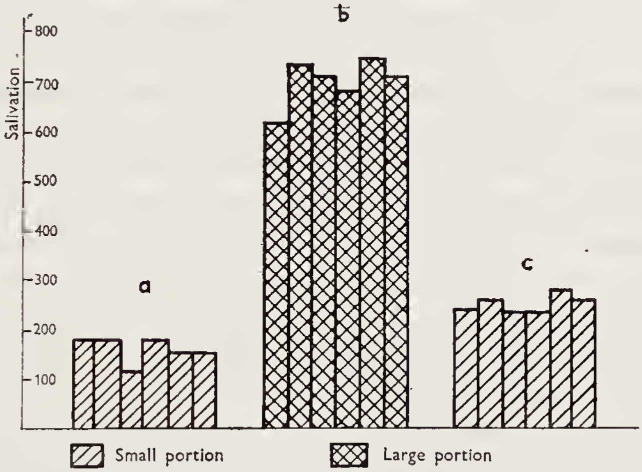


FIG. 7. Diagram showing the magnitude of salivary reflexes in a dog to portions of 10 g of powdered dried meat and bread before (a), and after (c), a series of experiments using 50 g portions (b).

In order, however, to interpret, in the light of the concept of the tonic conditioned reflex, both these data and the previously described new data regarding the elaborated switching of differently reinforced and differently delayed conditioned reflexes, we consider it necessary to say a few words about our theory of the mechanism which determines the increase or decrease in the magnitude of positive conditioned reflexes, as well as the duration of their latent period.

Taking into account some of the latest advances in the general physiology of excitable tissues, and on the basis of these and some of our other data, we propose a theory which is in accord with one of the principal hypotheses of modern neurophysiology, the development of which we owe primarily to British physiologists. We refer to the hypothesis that the intensity of nervous processes is determined mainly by the number of activated units. In complete agreement with this, we believe that the strength of unconditioned and conditioned reflexes in a normal organism is chiefly determined by the number of functioning nervous units, i.e. by the number of nerve cells in the cortical points of the corresponding stimuli which are reflexly activated by these stimuli. All other conditions being equal (level of excitability, duration of the stimulus, etc.), the stronger the unconditioned and neutral stimuli, the greater, within certain limits, will be the number of component elements of the conditioned connections which arise between them in the course of their combined action, i.e. the greater is the potential power of these connections. A change in the magnitude of an elaborated conditioned reflex caused by a protracted change in the magnitude of the unconditioned reinforcement may be regarded largely as an expression of a change in the number of functioning units in the cortical point of the unconditioned reflex, and subsequently in the conditioned connection. This would also seem to explain satisfactorily all other known phenomena relating to changes in the magnitude of conditioned reflexes in response to changes in conditioned and unconditioned stimuli which occur either separately or simultaneously, in either the same or opposite directions.

We shall now attempt to apply these concepts to the interpretation of the above-described data concerning tonic conditioned reflexes elaborated in response to different magnitudes of food portions as well as data concerning switching of differently reinforced and differently delayed conditioned reflexes.

The increase in the magnitude of the salivary reflex to a small portion of food (10 g) after many days of feeding the dog large portions (50 g) of the same food, we interpret as follows. Under practically identical experimental conditions and degree of alimentary excitation of the dogs, the small portion of food excites considerably fewer nerve cells in the cortical point of the unconditioned alimentary reflex (ring B in Fig. 8) than does the large portion of the same food (ring A). Systematic feeding of the dog for many days with a large portion of food under stable experimental conditions produces in the dog a tonic alimentary conditioned reflex of an intensity appropriate to the environmental factors, i.e. a tonic conditioned reflex increase in the excitability of an adequate number of cells (ring A) in the cortical point of the unconditioned alimentary reflex. After a transition from large to small portions of food, this heightened tonic conditioned reflex excitability of an inappropriately large number of cells in the cortical point of the unconditioned reflex, makes the reflex to these small portions more intense than before. Subsequently this increase in intensity of the reflex to small portions of food gradually diminishes and disappears for lack of reinforcement of the tonic conditioned reflex with large portions of food.

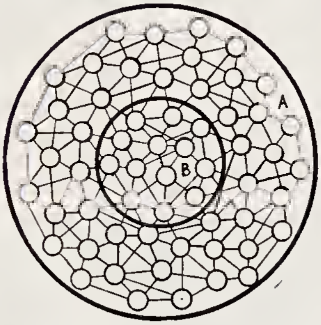


FIG. 8. Diagram showing a tonic conditioned alimentary reflex to experimental environment.

We explain the results of our experiments with the elaboration of differently reinforced conditioned reflexes as follows. In the chamber where the dog receives large portions of food the number of nerve cells in the cortical representation of the alimentary unconditioned reflex which are stimulated is greater than in the chamber where the dog receives small portions of the same food (in Fig. 9 they are designated by ring A and its counterpart, ring B). In each chamber, corresponding to the intensity of the alimentary unconditioned reflex, we eventually elaborated two types of conditioned reflexes: *tonic* conditioned reflexes to the switching agent, i.e. to the specific conditions of the chamber itself, and *phasic* conditioned reflexes to the specific, short-acting stimuli (in the figure the tonic connections with chambers I and II are designated by the thick arrows *a* and *b*, while the phasic conditioned connections are designated by vertical broken lines). When, after elaboration and stabilization of the conditioned reflexes, the experiment is performed in chamber I, the strong tonic conditioned reflex becomes active at once: in the cortical structures of the food center there appears a stable local excitation comparable in strength to the unconditioned reflex excitation in this center evoked by the presentation of large portions of food (ring A). Because of this a change takes place at the same time in the functional state of the phasic conditioned connection of corresponding intensity. When, on the other hand, the experiment is performed in chamber II, it is the weaker tonic conditioned reflex which becomes active: in the cortical structures of the food center there appears a local excitation comparable in strength to the unconditioned reflex excitation in this center evoked by the small portions of food (ring B). Because of this a change also takes place in the functional state of correspondingly fewer component elements of the phasic conditioned connection. For this reason, the same phasic conditioned stimulus, when acting in chamber I, i.e. against the background of the larger tonic alimentary conditioned reflex, evokes the larger phasic conditioned reflexes, and when acting in chamber II, i.e. against the background of the smaller

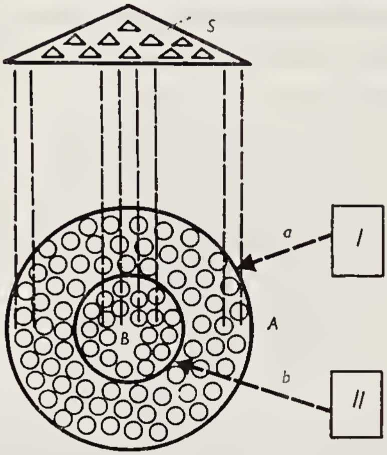


FIG. 9. Diagram representing the switching of differently reinforced homogeneous conditioned reflexes of the same kind.

tonic alimentary conditioned reflex, produces the smaller phasic reflexes.

It is more difficult to explain the data concerning the switching of differently delayed conditioned reflexes. This is due to the fact that in general it is not easy to imagine clearly, and especially to present graphically, the phase of inhibition of a positive conditioned connection which precedes the phase of its excitation and which is known as delayed inhibition in the same kind of conditioned reflexes or as the "latent period" of moderately delayed conditioned reflexes. Moreover, the question of the localization of conditioned inhibition in the links of the arc of a conditioned reflex still remains unsolved. On the basis of certain data (which will be dealt with in Chapter 6. Ed.), we believe that conditioned inhibition, including its variations mentioned above, arises in the elements of the conditioned connection itself and not in the cells of the cortical point of the conditioned stimulus, as Pavlov supposed, nor in the cells of the cortical point of the unconditioned stimulus, as some of Pavlov's pupils believe. If this is the situation as regards the more elementary phenomena, is it then surprising that we are at present still unable to explain at all convincingly the much more complex phenomenon of switching in differently delayed conditioned reflexes? All we can say now (this should not, however, be regarded as our explanation of the phenomenon) is that in the switching of differently delayed conditioned reflexes, a tonic conditioned reflex is elaborated to those functional states of the elements of the conditioned reflex arc which are similar in sign and different in duration, and which are evoked by a moderate delay of reinforcement in chamber I and by a longer delay in chamber II, leading finally to different durations of the initial phase of inhibition of the conditioned reflex.

It goes without saying that the above diagrams, like the theories on which they are based, cannot be considered thoroughly substantiated by experimental data; so far they are only of a hypothetic nature. We believe nevertheless that at the present stage of research into this problem they appreciably facilitate the generalization and interpretation of the available experimental material and pave the way for its further experimental and theoretical elaboration.

In conclusion, I should like to touch upon one more question. Today we are inclined to believe that the presence of tonic conditioned reflexes is not peculiar to switching alone, but represents a universal phenomenon of higher nervous activity in general. Even under ordinary experimental conditions such factors as the moment when the animal is brought to the laboratory, the appearance of the experimenter, the placing of the animal in the chamber, the preparations for the experiment, the stable environmental elements in the chamber – all of these factors together represent a highly complex and linked tonic conditioned stimulus which activates the cortex in a specific way and creates in the cortex a stable conditioned reflex background for subsequent phasic conditioned reflex activity. In other words, the same process takes place here as in our experiments with elaborated switching under the action of specially selected switching agents. Amid the great diversity of inborn reflex activity of the nervous system, neurophysiologists long ago demonstrated the existence of two interconnected forms of this activity, namely, tonic reflexes and phasic reflexes, which have specific characteristics and are of definite significance for the various functions of the organism. In our opinion, there are at present sufficient grounds to assume that amid the great diversity of conditioned reflexes which constitute the higher or psychic activity of the system, there also exist both phasic and tonic conditioned reflexes which likewise have specific characteristics and are of definite significance for this activity. Precisely in this light we consider our data in regard to switching, as well as our theories concerning tonic conditioned reflexes, as new corroboration of one of the fundamental principles of modern physiology which has been mentioned above, and according to which the laws governing the activity of various parts of the central nervous system have common biological roots. It is the principle which was characterized by Pavlov as the "natural community of basic relationships."

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CHAPTER 5

SOME ASPECTS OF THE CLOSURE OF CONDITIONED CONNECTIONS AND THE DEVELOPMENT OF THEIR CHARACTERISTICS

ALTHOUGH much has already been achieved in the field of conditioned reflexes by I. P. Pavlov and his pupils and by his other followers in many countries of the world, nevertheless many aspects of this problem have not yet been satisfactorily investigated and need further experimental research and theoretical study. Many scientists in the U.S.S.R. and elsewhere are studying the elaboration of conditioned reflexes, the development of their characteristics, their stabilization and the significance of various factors favorable to these processes.

At present the main focus of our own experimental and theoretical investigations in this field (Asratian 1952, 1955, 1958) is on studying the role of the strength of stimuli and the sequence of their application in the elaboration of conditioned reflexes and the development of their characteristics. The important role played by the relative strengths of the excitatory processes which take place in nerve structures and especially in the cortex, is generally known. Pavlov (1949b) stated: "Prime importance must, of course, be ascribed to the intensity of excitatory relations in the activity of the cerebral cortex." He also repeatedly emphasized the great importance of the temporal pattern of pairing of stimuli for the elaboration of conditioned reflexes. He stated (1949a) in particular, that "since conditioned stimuli play the role of signals, they can become effective only when they precede the physiological activity being signaled."

Our collaborators investigated these problems in dogs in the usual semi-soundproof chambers designed for the study of conditioned reflexes. In order to elaborate conditioned reflexes with definite functional characteristics, we paired in various ways either two so-called "indifferent" stimuli, two different unconditioned stimuli, or one "indifferent" and one unconditioned stimulus. The characteristic feature of our experiments was the attempt to select and apply only those "indifferent" stimuli which produced in experimental animals reflex reactions that could be objectively observed and graphically recorded.

Our collaborators M. E. Varga and Ia. M. Pressman (1958) performed a series of experiments on dogs in which they paired two so-called "indifferent" stimuli, namely, a tone and a passive lifting of the animal's leg. In some of these experiments stimuli were always applied in the same stereotyped sequence, in others in a variable sequence. The advantage of using a passive movement of the leg as one of the "indifferent" stimuli is that it gives a direct and immediate indication of the associative connections between the paired stimuli by means of objective recording of indices such as active movement of the paw or an electromyogram of its muscles. In addition, with these indicators the investigators were able to study directly the whole process of the closure of conditioned connections when the stimuli were paired, from the very beginning of the connections to any subsequent stage of their evolution.

In experiments by previous investigators of this problem (Narbutovich and Podkopaev, 1936; Zelenyi, 1928; Oreshuk, 1950; Rokotova, 1952; Karmanova, 1955; Bregadze, 1956; Sergeev, 1957; and others) this was not possible, because they used only a method of indirect and also sporadic indication of the process of closure of associative connections between "indifferent" stimuli. Data obtained by Varga and Pressman showed clearly that not only during the variable sequence of pairing of tones with the passive lifting of the paw, but even with the stereotyped sequential pairing, there developed between the cerebral foci of representations of these stimuli a bidirectional* "associative connection," i.e. a truly conditioned reflex connection (Fig. 1). Moreover, in the course of their experiments, Varga and Pressman also obtained data which in part confirm findings previously demonstrated by other workers, and in part are new. For example, in agreement with the findings of other authors, they showed that the connections between "indifferent" stimuli are characterized by extreme fragility and instability. After being established, they rapidly begin to weaken and soon disappear after a period of more or less regular functioning. They recover again very briefly but only after an interval, either during the experiment or when an alimentary conditioned reflex has been elaborated in response to one of the paired stimuli.

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* See editor's footnote in Chapter 4.

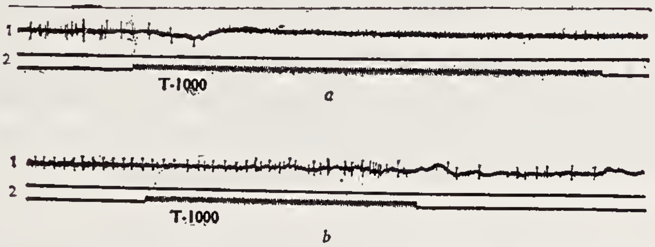

FIG. 1. Conditioned connections resulting from various pairings of a tone and the passive lifting of the dog's hind leg. (a) active lifting of the leg (indicated by the decrease in frequency or the disappearance of the electric potentials in the extensor of the leg, the gastrocnemius muscle) in response to a tone after 37 pairings with a passive lifting of the leg in the stereotyped sequence "tone — passive lifting"; (b) reaction to a tone after 28 pairings of a passive lifting of the leg with this tone in experiments with a reverse sequence, i.e. "passive lifting — tone". 1, electromyogram of the gastrocnemius muscle; 2, conditioned stimulation.

At the same time the experiments of Varga and Pressman demonstrated other findings which illustrate the great significance of a definite sequence in pairing stimuli. Their experimental data demonstrate that although the above-mentioned features, fragility and instability, are characteristic of both conditioned connections between the cerebral foci representing the two stimuli, they do not pertain equally to these reflexes. When a tone paired with the passive lifting of the animal's leg were applied in a variable sequence, the conditioned connections arising between them are almost identical in their rate of formation, consolidation, stability, resistance to extinction, etc. But when these stimuli are paired in a stereotyped sequence, the resulting conditioned connections differ significantly from each other in all of these repects. A direct conditioned connection, i.e. a connection leading from the preceding (P) to the subsequent (S) stimulus is more easily elaborated and is stronger and more resistant to extinction and other altering factors than is a reverse or backward conditioned connection, i.e. a connection leading from S to P. Moreover, a direct connection recovers more rapidly than a reverse after a sharp extinction or when, after the natural disappearance of the connections, an interruption is made in the experiment, or when one of the paired stimuli becomes an alimentary conditioned signal. Essentially similar results were obtained by Varga and Pressman in a series of experiments on other dogs in which they paired passive lifting of the animal's leg with puffs of air into its eye, which evoked the blinking reflex. The advantage of the pairing of these two stimuli over those applied in the previous experiments was that both stimuli (not just one) evoked effects which could be objectively recorded. Moreover, as shown in the course of the experiments, the new stimulus (air puffs into the animal's eye) applied in this combination, proved stronger than the stimulus (a tone) applied in the previous combination. With this technique it was possible to demonstrate the elaboration of direct and reverse connections in a more distinct, graphic and, which is especially important, direct, form. This was possible both

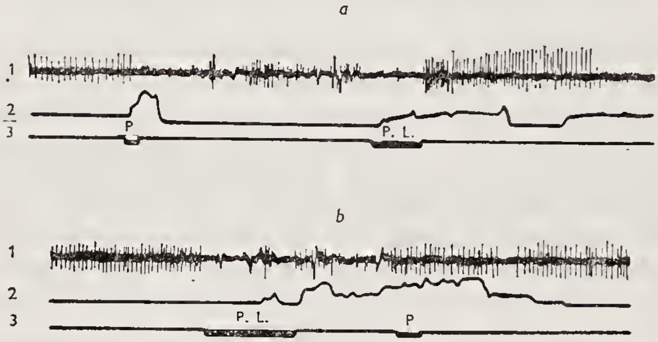

FIG. 2. A bidirectional connection resulting from the pairing of a passive lifting of the leg with application of air puffs to the eye. (a) Conditioned motor reflex appearing when paired stimuli are applied in the stereotyped sequence "air puffs — passive lifting." In response to air puffs P the dog blinks and lifts the leg, as indicated by the disappearance of action potentials in the gastrocnemius muscle. The lifting of the leg P.L. is again accompanied by blinking, which indicates a reverse connection. (b) A conditioned eyelid reflex appearing when the paired stimuli are applied in the stereotyped sequence "passive lifting — air puffs." In response to the passive lifting of the leg P.L. the dog blinks. After air puffs into the eye P there is observed, along with the blinking, the disappearance of action potentials in the gastrocnemius muscle, which indicates a reverse connection. 1, electromyogram of the gastrocnemius muscle; 2, eyelid movement; 3, stimulation.

when one of the paired stimuli was applied first in a stereotyped sequence, and also when the other stimulus was applied first (Fig. 2). Just as air puffs into the animal's eye proved to be a stronger stimulus than a tone, so the direct conditioned connections were much more stable than when a tone was combined with the passive lifting of the animal's leg. To some extent this also applies to reverse conditioned connections.

New data related to this problem were demonstated by Liang Ji-An (1958), who continued the investigation of a very important question which Varga (1953) had previously studied in our laboratory.

Using dogs, Varga paired in a strictly alternating sequence two classical unconditioned stimuli of moderate intensity, namely offering electric stimulation of a leg. She demonstrated the possibility of elaborating a stable bidirectional conditioned connection between the cerebral nervous structures corresponding to these two stimuli. It should be noted that under standard experimental conditions (strictly alternating sequence of the pairing of stimuli, relative equality, of their intensity, observance of routine maintenance of the experimental animal, etc.) these conditioned connections are practically equal as regards sign, strength, stability, etc.

On the other hand, in the experiments of Liang Ji-An, the very same unconditioned stimuli were paired in a stereotyped sequence in naive dogs. In other words, he paired in a stereotyped sequence a defence motor reflex of a foreleg, evoked by an electric shock of moderate intensity, with an alimentary reflex to the presentation of a medium size portion of powdered meat and bread. In one series of experiments performed on a group of dogs, the application of the electric shock preceded the offering of food, while in another series, performed on another group, the offering of food preceded the application of the shock. Both series of experiments gave essentially the same results, which in some respects agree with the data of Varga and of Pressman and Varga, but which differ on some essential points. In the experiments of Liang Ji-An also, bidirectional conditioned reflex connections between the cerebral foci representing the paired unconditioned stimuli were formed (Figs. 3 and 4). Here also, however, as in the similar Varga and Pressman experiments, direct and reverse conditioned connections between these foci were far from equal. Moreover, compared to Varga and Pressman's experiments,

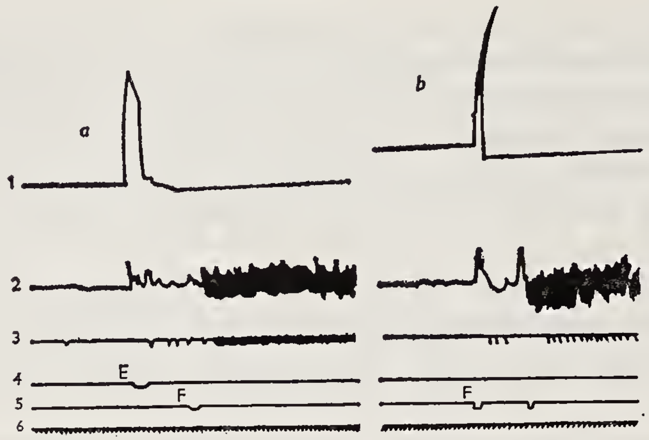

FIG. 3. Alimentary conditioned reflex to an electric current. A dog to which an electric current and the offer of food were applied in the stereotyped sequence "electric current — food." (a) a conditioned salivary alimentary reflex to the application of electric current (direct connection); (b) movements of the leg during offer of the food container (reverse connection). Lines from top to bottom: 1, mechanogram of movements of the left foreleg; 2, mechanogram of chewing movements; 3, salivation in drops; 4, electric shock; 5, food presentation; 6, time in sec.

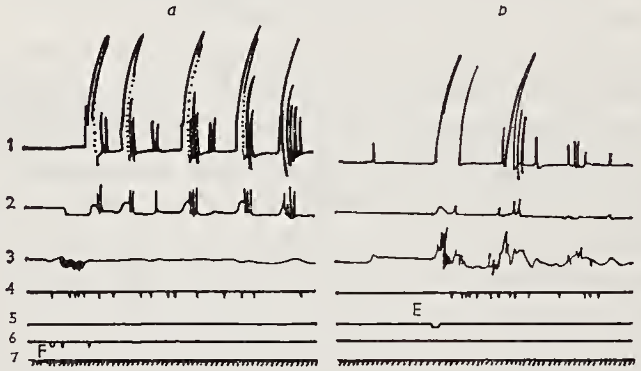

FIG. 4. Electrodefence motor reflex to offer of food. A dog to which the offer of food and electric current were paired in the stereotyped sequence "food — electric current." (a) a conditioned motor defence reflex to termination of the act of eating (direct connection); (b) a conditioned alimentary reaction to the electric current (reverse connection).

Lines, top to bottom: 1, mechanogram of movements of the left foreleg; 2, mechanogram of movements of the right foreleg; 3, mechanogram of chewing movements; 4, salivation in drops; 5, electric shock; 6, food; 7, time in sec.

those of Liang Ji-An showed a considerably more marked difference in the rate of closure, formation and stabilization of conditioned connections between those leading from the preceding (P) to the subsequent (S) stimulus, and those from S to P. In both series of Liang Ji-An's experiments, the direct conditioned reflex connection between the paired unconditioned stimuli is formed slightly more rapidly than is the reverse conditioned reflex connection. This connection is also of much greater strength and stability and is characterized by a considerably greater regularity than is the reverse connection. A direct conditioned reflex connection between two unconditioned, i.e. physiologically strong, stimuli (in contrast to a direct connection between two indifferent, i.e. physiologically weak, stimuli) forms easily, becomes regularly stabilized from day to day, and persists while the conditions which gave rise to it are maintained, namely, while the stimuli are paired in the same sequence.

The situation is entirely different with reverse conditioned reflex connections between these unconditioned stimuli. They strongly resemble conditioned connections between indifferent stimuli, especially in their fragility and irregularity. It must be pointed out that a reverse connection is so weak, so unstable, multiphasic and varied in its manifestations and depends on so many factors for its functioning, that we initially even doubted its conditioned reflex nature.

Some of the peculiar features revealed by the experiments of Liang Ji-An in the functioning of reverse conditioned reflex connections, are of special interest. For example, S more easily evokes the reflex corresponding to P if the intensity of P is increased or if the excitability of the central nervous structures is raised. By intensifying P or by raising the excitability of the appropriate nervous apparatus, it becomes possible to revive and activate the reverse conditioned connections even after they have ceased to appear under the usual experimental conditions. A similar result is obtained if S is weakened or the excitability of the corresponding central nervous structures is lowered. For example, in an experiment in which stimuli are applied in the sequence "shock—food," the offering of food evokes a conditioned reflex lifting of the animal's leg more frequently and more distinctly if the leg has previously been stimulated by a stronger shock than usual or if, prior to the experiment, the dog was fed to satiety. The feature common to these two different preliminary experimental manipulations is that they both result in the same picture of the relative excitability or excitation of the central nervous structures corresponding to the two stimuli.

In contrast to this, a preliminary intensification of S or an increase in the excitability of the nervous structures corresponding to its reflex, results in the inactivation of the reverse connection even when they are functioning regularly and satisfactorily under the usual experimental conditions. Similar results are obtained by a preliminary weakening of P or by a preliminary decrease in the excitability of the appropriate nervous structures. Let us, for example, again take the type of experiment thoroughly studied by Liang Ji-An in which the stimuli were applied in the sequence "shock – food." Here the offering of food evokes no conditioned lifting of the leg if the animal is in a fasting condition before the experiment, if it is given appetizing food at the start of the experiment, or if its leg has first been stimulated by a weak electric shock. It may be noted that, although these preliminary experimental manipulations are different, they have this in common: they result in different ways in the creation of the same picture of the relative excitability or excitation of the central nervous structures corresponding to these two stimuli.

Related to the problem under discussion are new and interesting data obtained by our co-worker M. I. Struchkov (1958). In experiments designed for the elaboration of conditioned reflexes in dogs, he utilized a sequence of pairing the "indifferent" with the conditioned stimuli, which is known in the literature as "covering", i.e. the "indifferent" stimuli are applied after the beginning of the action of the unconditioned stimulus. Struchkov used food as the unconditioned stimulus and chose only those "indifferent" stimuli which in themselves evoke in the organism specific reactions that can be objectively observed and recorded. For example, in one series of experiments he used the passive lifting of one of the dog's hind legs, and in another a brief cooling of a limited area of the skin on one side of the animal's body which evoked a local vasomotor reaction. This sequence of stimuli was used systematically in all the experiments of each series. The following very interesting findings appeared. After the repeated pairing of an alimentary reflex with one of the "indifferent" stimuli, the offering of food alone began to evoke a conditioned reflex type of reaction specific for these stimuli, i.e. in one series of experiments the reaction was an active lifting of the paw and in another a local vasomotor reflex (Figs. 5a and 6). In other words, in Struchkov's experiments the classical unconditioned stimulus, food, played the role of a conditioned or signalling stimulus, while the so-called "indifferent" stimuli, passive movement of the leg or local cooling of the skin, appeared as reinforcing stimuli. These remarkable experiments demonstrate that it is precisely the position in time of the

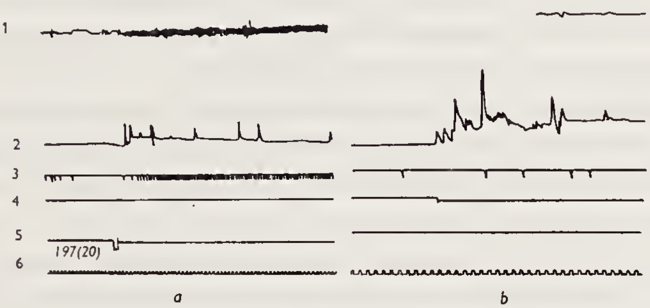

FIG. 5. (a) A conditioned motor reflex evoked in the dog by the act of eating (direct connection); (b) alimentary reflex evoked by the passive lifting of the leg (reverse connection).

1, chewing movements; 2, movements of the same leg; 3, salivation; 4, passive movement of the leg; 5, food (figure indicates the number of pairings); 6, time in sec.

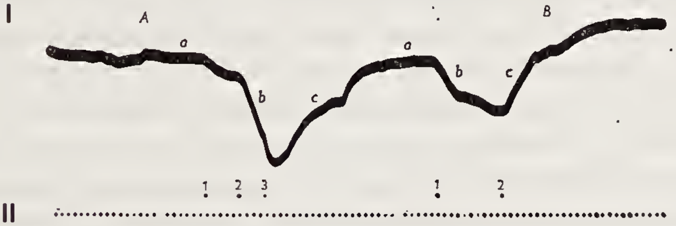

FIG. 6. Conditioned and unconditioned reflex changes in local skin temperature.

(A) Decrease of skin temperature of the dog under the influence of food for 60 sec and the subsequent application of cold. I, record of skin temperature. II, time, 12 sec; (a) background; (b) decrease of temperature during the process of eating and the application of cold; (c) return of skin temperature after the process of eating and the effect of cold. 1, offer of food and start of the act of eating; 2, application of cold; 3, termination of eating and application of cold.

(B) Conditioned reflex decrease of skin temperature during the process of eating. (a) background; (b) decrease of skin temperature during the process of eating; (c) return of skin temperature after the process of eating. 1, offer of food and start of the process of eating; 2, termination of eating.

preceding stimulus (P) which determines the acquisition by food of the properties of a signal in relation to other reflexes, i.e. the formation in one case of a somatomotor conditioned reflex to the offering of food, and in the other case of a vasomotor conditioned reflex. It may be assumed, therefore, that this is the result of the formation of a direct conditioned reflex connection between the central nervous structures of the alimentary reflex and the corresponding structures of the somatomotor or vasomotor reflexes.

It was subsequently demonstrated that in these experiments there also arises a bidirectional conditioned connection between the unconditioned and indifferent stimuli when these are paired in a definite, stereotyped sequence. This means that with the direct conditioned reflex connection there exists a reverse connection which conducts impulses from the nervous structures corresponding to S (i.e. to the movement of the leg or the local cooling of the skin), to the nervous structures corresponding to P (i.e. the alimentary stimulus). This is evident from the observation that the passive lifting of the leg or the local cooling of the skin also acquire the properties of a signal (i.e. the faculty of evoking an alimentary reaction in a conditioned reflex manner) when repeatedly paired with food, following the "covering" method used in the experiments discussed above (Fig. 5). The data obtained from these experiments demonstrate that here, too, there is a considerable difference between the specific characteristics of direct and reverse conditioned connections, and that, furthermore, it is the same kind of difference as is observed when two "indifferent" or two unconditioned reflexes are paired. Thus, in this case the direct conditioned reflex connection is formed more rapidly than the reverse conditioned reflex connection and is much more intense, stable and effective.

The finding demonstrated by Struckov that "covering" indifferent stimuli with unconditioned reflexes results in the formation of weak and unstable conditioned reflexes, has been known ever since the investigations of Pimenov (1908), Kreps (1933), Pavlova (1933), Vinogradov (1933), Petrova (1933), and others, but these authors regarded it as an indication of the elaboration of a usual one-way conditioned reflex connection with certain specific characteristics. In Struchkov's experiments this finding appears in quite a different light, namely, as a particular case of the general phenomenon of closure of a reverse conditioned reflex connection (side by side with the direct connection) when two stimuli are paired in a stereotyped sequence. The transitory character of this connection, which was pointed out long ago by many scientists and was regarded by Pavlov as an enigmatic phenomenon in conditioned reflex activity, may to a considerable degree be interpreted as the result of its systematic non-reinforcement during the periodic application of a stimulus for the purpose of developing a conditioned reflex.

The significance of a definite time sequence in the pairing of stimuli for the closure of new conditioned reflex connections and for the preservation of those which already exist, is illustrated by the experimental data obtained by our co-worker B. I. Pakovich (1956, 1957).

From earlier investigations by a number of American psychologists (Schlosberg, 1928; Hilgard, 1937; Wolfle, 1930; Bernstein, 1934; and others) which were performed on human subjects, it was known that when the indifferent stimulus precedes the unconditioned stimulus by 0·1 sec or less, the elaboration of a conditioned reflex is impeded and sometimes even becomes impossible.

In recent years Pakovich made a thorough study of this question with motor reflexes in dogs, which can be objectively recorded with a sensitive mechanographic device and also in some experiments by electromyography. His data demonstrate that when the pairing of a tone of moderate intensity with electric stimulation of a leg is used, a motor conditioned reflex is not elaborated in the animal if both stimuli start and stop acting strictly simultaneously for a period of 1–5 sec. According to Pakovich's findings, hundreds of pairings of these stimuli do not lead to the formation of the expected conditioned reflex even when the tone precedes the electric current by up to 100 msec but when their action stops simultaneously. The picture does not change if the intensity of the stimulating current is considerably increased. A conditioned reflex is elaborated only when the interval between the start of the tone and that of the electric stimulation of the skin exceeds this time limit (Fig. 7). Pakovich also demonstrated that the latent period of the newly formed conditioned reflex, as well as its intensity, duration, stability and other characteristics depends to a considerable degree on the interval between the starting times of the two stimuli.

Pakovich demonstrated another very interesting phenomenon: a firmly stabilized and regularly evoked electric motor defense reflex in dogs disappears if the conditioned stimulus is applied strictly simultaneously with the unconditioned stimulus in the course of a series of experiments. This also occurs when the interval between the onsets of the conditioned and unconditioned stimuli is reduced to 100 msec. The conditioned reflex reappears only when these conditions of the combined action of both stimuli are changed and when the interval between the onsets of the two stimuli again exceeds 100 msec. The restoration of the conditioned reflex proceeds more rapidly and is more complete when this interval is somewhat greater than its threshold value.

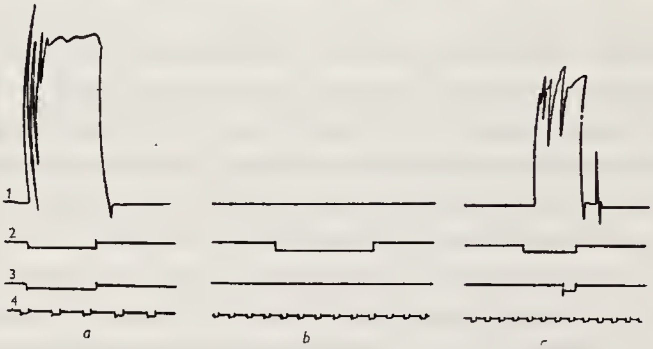

Fig. 7. Motor reflexes resulting from different pairings in time of two stimuli, a tone and an electric current. (a) motor reaction resulting from the strictly simultaneous action of the stimuli; (b) absence of conditioned reflex to the tone after 582 strictly simultaneous pairings with an electric current; (c) appearance of a conditioned reflex to the same stimulus after 14 pairings with an electric current with a delay of 2 sec.

1, movements of the leg; 2, conditioned stimulation; 3, unconditioned stimulation; 4, time in sec.

On the basis of numerous investigations from Pavlov's laboratories, it is known that conditioned reflexes can become weakened or may even disappear as a result of "covering" the conditioned stimuli with the unconditioned stimulus. Although in Pakovich's experiments the stimuli were paired in a manner different from that utilized in "covering," nevertheless the possibility is not excluded that there may be something in common between these two phemonena.

Pakovich recently carried out an experimental analysis of the disappearance of the previously developed conditioned reflex when the conditioned and unconditioned stimuli were applied simultaneously. He found this phenomenon was caused by the sporadic, isolated application of the conditioned stimulus in experiments for the purpose of demonstrating its conditioned effect. It seems, therefore, that the strictly simultaneous application of the conditioned and unconditioned stimuli results in such a weakening of the conditioned reflexes that they disappear after only a few and infrequent applications of the conditioned stimulus without reinforcement.

It is noteworthy that, although the strictly simultaneous application of both stimuli or a certain definitely minimal interval between their starting time produces such a rigid temporal regimen in the activity of the cerebral structures that it eliminates the possibility of coupling new conditioned connections and even abolishes all previously formed stable conditioned reflexes; nevertheless, this does not preclude the possibility of a negative and even a positive interaction between the cerebral structures which correspond to these stimuli. Pakovich demonstrated that even under the conditions of the strictly simultaneous action of a tone and electric current, there may take place both a reciprocal inhibition as well as a summation of the excitation caused by each of these stimuli in the corresponding central nervous structures. The reciprocal inhibition is chiefly observed in the first period of the paired action of the stimuli, when the orienting reaction to the tone is still strong. The summation of excitation is chiefly observed in the late periods of the paired application of these stimuli. During these periods a subthreshold excitation evoked by the isolated application of the electric stimulation becomes a superthreshold excitation when an electric current of the same intensity is applied together with a tone. Under the same conditions of the paired action of both stimuli, a weak superthreshold excitation evoked by a weak electric current becomes considerably intensified, etc. Finally it must be noted that, according to Pakovich's data, the phenomena described above and the determining factors observed in the formation of conditioned reflexes are not connected in any appreciable degree with the age or typologic characteristics of the experimental animals, and thus it follows that they are related to the category of basic phenomena and determining factors which are characteristic of the conditioned reflex activity of the higher parts of the central nervous system.

How are all these findings to be interpreted and generalized?

Experimental psychologists and neurophysiologists as well as animal trainers have long known a number of facts which demonstrate the formation of a bidirectional nervous connection and which provided a basis for the formulation of corresponding theories on this question (F. Goltz, 1884; V. M. Bekhterev, 1887; H. Ebbinghaus, 1911–1913; O. Kalischer, 1912, 1914; A. A. Savich, 1913; G. P. Zelenyi, 1929; I. S. Beritov, 1932; Iu. M. Konorskii and S. Miller, 1936; I. O. Narbutovich and N. A. Podkopaev, 1936; I. S. Rosenthal, 1936; M. K. Petrova, 1941; P. S. Kupalov, 1948; V. K. Fedorov, 1952; L. G. Voronin, 1952; and others). In this connection special mention must be made of the theories of I. P. Pavlov (1949c) concerning bidirectional conditioned connections, proposed by him and based on original observations made in his laboratories. He believed that "when two nerve points are connected or associated, the nerve processes developing between them proceed in both directions." At that time, however, the founder of the theory of conditioned reflexes believed that the important question of bidirectional conditioned connections was still not sufficiently developed experimentally or theoretically, and that it required further study. It seems to us that the data recently obtained in our laboratory increase to some degree our knowledge of this problem. They reveal new aspects of direct and reverse connections and, especially, new aspects of the role played in this process by the physiologic intensity of the stimuli and by the sequence of their pairings.

All these findings, in addition to the previously known data of other scientists, lead to the conclusion that the formation of a bidirectional conditioned connection is not a limited phenomenon peculiar only to a certain group of conditioned reflexes, but is widespread, if not universal, for this class of reflexes. This forms a structural basis, so to speak, for a bidirectional functional connection and for a circular conditioned reflex interaction between the connected nerve points, in approximately the same manner as was postulated by Lorente de No (1934, 1938) and his school for the activity of the central nervous system in general. In any case, there is an adequate basis for this theory during the stage of formation of the conditioned reflexes and during the initial period of their functioning. Subsequent evolutionary development, depending on a number of circumstances, leads to different results: to the inhibition of both conditioned connections, to the inhibition of one of them, and sometimes to the preservation of one or the other of these connections in a state of stability and efficiency. In that case the usual one-way conditioned connection may be regarded as a derivative of a bidirectional conditioned connection, as a result of the subsequent inhibition of one of the paired connections.

We are, of course, at present far from a satisfactory interpretation of these findings, but some purely hypothetical statements may nevertheless be made. Specifically, we are inclined to believe that the closure of a bidirectional conditioned connection may be accounted for by the relatively equal intensity of the excitations which arise in the corresponding central nervous structures under the influence of the paired stimuli. This basic condition can best be observed when two stimuli of almost equal physiologic intensity are paired (for example, two "indifferent" stimuli, two unconditioned stimuli, or one "indifferent" and one unconditioned stimulus), and when the two paired stimuli are cimbined in a variable sequence. Such a combination of the two factors can ensure the closure and maintenance of bidirectional conditioned connections with components equivalent in all respects. When, however, these paired stimuli are combined in a stereotyped sequence, the basic condition is not fulfilled and this, in our opinion, leads to the development of non-equivalence in the direct and reverse conditioned connections. We explain this as follows. When the P and S stimuli are applied in a stereotyped sequence, the central nervous structures corresponding to S become more excited after the appearance of the conditioned connections than do the central nervous structures corresponding to P. This is due to the fact that the structures corresponding to S are in this case stimulated by two sources: by P in a conditioned reflex way and by S in an unconditioned reflex way. This leads to a disturbance in the initial relative equality of intensity in the excitation of the central nervous structures corresponding to the paired stimuli. Consequently the excitation of the nervous structures of S dominates to a large extent the excitation of the nervous structures corresponding to P, and thus the direct conditioned connection starts to dominate the reverse connection in all respects. The correctness of this explanation was confirmed by Varga in a special series of experiments (1958) in which she demonstrated that the transition from a variable sequence of paired stimuli to a stereotyped sequence causes a considerable increase in the excitability of the central nervous structures which correspond to S and their domination in this respect over those corresponding to P.

We are inclined to offer a similar explanation for Struchkov's findings concerning the transformation of food into a signaling stimulus for somatomotor and vasomotor reflexes. In the first phase of pairing food (as a preceding stimulus P) with the passive lifting of the paw or a local cooling of the skin (as a subsequent stimulus S), the central nervous structures corresponding to the subsequent stimulus become relatively highly excited on account of the novelty of the stimulus to the experimental animals. Because of this, the level of excitation of the central nervous structures corresponding to these stimuli approaches the level of excitation of the central nervous structures of the alimentary reflex, which is the preceding stimulus. This creates favorable conditions for the closure of the double conditioned connection between these structures. Subsequently, after the closure of this double connection, the above-mentioned factor takes effect, namely, a more intense excitation of the central nervous structures of S which comes as a summation from two sources: first, from the food in a conditioned reflex way, and then, against this background, from an adequate stimulus (lifting the paw or cooling the skin) of the nervous structures in an unconditioned reflex way. This maintains the previously created relative equality in the levels of excitation of the nervous structures corresponding to the paired stimuli, i.e. the prerequisite necessary for maintaining the double conditioned connection is preserved.

Findings concerning the relatively different durations of efficiency for the conditioned connections which occur as a result of pairing various stimuli of different biological significance (two "indifferent" stimuli, two unconditioned stimuli, or one "indifferent" and one unconditioned stimulus), can best be understood by considering the important role of the concrete physiological strength of the paired stimuli. There are reasons to believe that this factor plays an important role in the development of the conditioned connections, whereas the relative intensity of excitation of the central nervous structures corresponding to these stimuli and the sequence of their application play an important role in the closure of these connections and the formation of some of their characteristics. If we assume that the level of excitation of the central nervous structures giving rise to conditioned reflex connections expresses approximately the number of functional units which are activated, and that the intensity of the conditioned reflex connection is its result, then the following conclusion can be drawn: for the maintenance and functioning of conditioned connections it is necessary that they have a certain threshold intensity, i.e. that they consist of a definite "threshold" number of functional units. Weak conditioned connections, that is, connections consisting of a small number of functional units, rapidly become fatigued and exhausted even after moderate activity, and a protective inhibition occurs which blocks them. At present we are unable to explain satisfactorily why such an inhibition develops in structures corresponding to weak conditioned connections. We may, however, point out with some justification that there is a similarity between this phenomenon and the rapid development of inhibition during prolonged activity of weak conditioned and even indifferent stimuli. This phenomenon has long been known from numerous investigations carried out by Pavlov in his laboratories. Moreover, the development of inhibition in connection with the prolonged activity of weak stimuli is apparently among the phenomena which are common to all nerve structures.

We cannot as yet give a satisfactory explanation for the data obtained by Pakovich, which demonstrate that a conditioned reflex cannot be formed when two paired stimuli act simultaneously. Nor can we explain the disappearance of an existing conditioned reflex when a conditioned and an unconditioned stimulus are similarly paired, although in this case there remains the possibility of a positive and a negative interaction between these stimuli. It is possible that a certain role in this regard is played by the mutual inductive inhibitory influences of the simultaneously excited cerebral structures. These influences, however, do not prevent the summation of excitations that have originated in them.

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CHAPTER 6

THE ORIGIN AND LOCALIZATION OF CORTICAL INHIBITION IN THE ELEMENTS OF THE CONDITIONED REFLEX ARC

THE very important coordinating role of inhibition in the integrative activity of the central nervous system, particularly its higher divisions, was demonstrated and described in detail by the classical neurophysiologists Sechenov, Sherrington, Pavlov, Vvedenskii, and their many successors. Also well known are the findings and theoretical propositions of Pavlov and his pupils pertaining to another important role of inhibition in the vital activity of the same system, namely, its protective and restorative role. In addition, modern physiology also has available to it a large body of data relative to the regular patterns of the origin of inhibition in nervous structures, its interaction with excitation, its dependence on various kinds of factors, the diversity of its manifestations, etc. But in spite of the unceasing and even accelerating progress of our knowledge about inhibition, many of its aspects still remain to be worked out, and neurophysiologists, following Pavlov, still refer with some bitterness to the "cursed problem" of inhibition.

Included among the questions pertaining to this problem that have not been sufficiently studied and remain largely unanswered is the question of the origin and localization of various types of cortical inhibition in the elements of the conditioned reflex arc. This chapter is concerned with precisely this question, and contains a brief presentation of several new findings obtained by my colleagues and myself, together with theoretical propositions that derive in large measure from these findings.

The question of the origin and localization of various kinds of cortical inhibition in the elements of the conditioned reflex arc has attracted the attention of investigators throughout the entire period of development of the theory of higher nervous activity. Most of this attention has been paid, and continues to be paid, to the development and localization of conditioned inhibition, that is, the form of inhibition that is specific to the cerebral cortex and its most important activity. Until recently there were, in the main, two opposing points of view concerning this question: (1) the position first set forth by Babkin (1904) and Zelenyi (1907), and later championed by Pavlov himself, that conditioned inhibition originates in the cortical nerve cells of the focus of the conditioned stimulus; and (2) the view advanced by Perelzweig (1907) and Kasherininova (1907), and later upheld by P. K. Anokhin *et al.* (1932), B. I. Khodorov (1955) and others, that conditioned inhibition originates in the nerve cells of the focus of the unconditoned stimulus.

The first viewpoint is supported mainly by the well known observation that conditioned inhibition is irradiated from the nerve structures of any one conditioned reflex to the nerve structures of other conditioned reflexes of the same type, and at times even to those of other types, i.e. the observation that this inhibition spreads to other related and even unrelated conditioned reflexes. In support of this point of view, A. I. Roitbak (1958) cites his own recent data demonstrating that when a conditioned reflex is extinguished, the character of the electric reaction of the cortical focus of the conditioned stimulus in response to the application of this stimulus changes markedly. In support of the second point of view no significant direct findings have been produced, but its correctness is usually argued on indirect grounds, especially those which indicate the unsoundness of the opposing viewpoint, i.e. the first viewpoint (they note, for example, the perception of the stimulus of the inhibited conditioned reflex, etc.).

P. S. Kupalov *et al.* (1933, 1955) postulated that conditioned inhibition develops simultaneously in the cells of the foci of both conditioned and unconditioned stimuli. Iu. M. Konorskii (1958) also recently developed the theory that cortical inhibition is a manifestation of the activity of special inhibitory structures which exist apart from, and parallel to, the structures of excitation at the cortical level, in somewhat the same way that they exist at the subcortical, spinal and other levels of integration in the central nervous system. Finally, we ourselves (Asratian, 1947, 1949, 1955) have expressed the theory that conditioned inhibition originates first in the elements of the conditioned connection itself, which we represent as a chain of internuncial neurones, and not in the cells of the foci of the conditioned or unconditioned stimuli as the advocates of the other theories believe. We admit, however, that when inhibition that has originated in elements of the conditioned connection becomes markedly intensified, it may subsequently also encompass the cortical nerve elements of the foci of both the conditioned and unconditioned stimuli. What findings and arguments, then, form the basis of this theory which, from all indications, is at present supported by certain other Soviet scientists, for example, G. V. Skipin (1957), F. P. Maiorov and his co-workers (1959), and others?

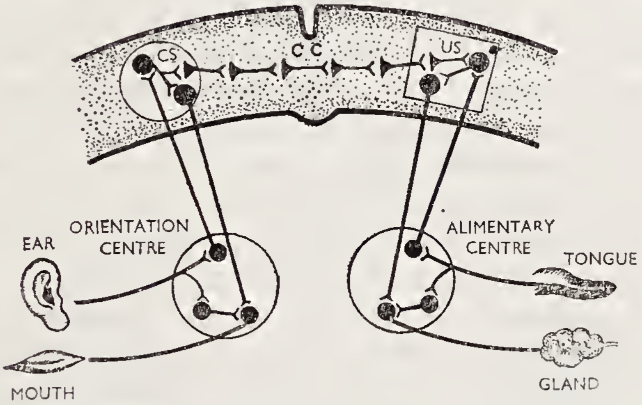

FIG. 1. Scheme of the conditioned reflex arc. CS, conditioned stimulus; US, unconditioned stimulus; CC, conditioned connection.

In order to make our account complete and preserve its chronological sequence, we must refer to data that have long been known and that other authors have often cited in connection with the question of the origin of conditioned inhibition in the elements of the conditioned reflex arc. I refer to the observation, mentioned above, of the perception of the conditioned stimulus and the reaction to it after the inhibition of the positive conditioned reflex, i.e. after its extinction, differentiation, delay, etc. This observation unquestionably indicates that inhibition which originates under these circumstances in the conditioned reflex arc and which results in blocking the conduction of excitation through it, is localized not in the cortical focus of the conditioned stimulus (CS in Fig. 1), but somewhere in the subsequent elements of the arc. This is obviously also indicated by data concerning the different courses of extinction or differentiation of the different components of the same conditioned reflex, for example, the extinction or differentiation of the salivary and motor components of the alimentary conditioned reflex.

It is well known that often one of the components of a conditioned reflex may be completely inhibited while a second continues to be evoked for a long time. Among the findings that have been generally known for many years, and which are of definite interest from the standpoint of the question we are here discussing, is that the unconditioned reflex does not change significantly upon the inhibition of the conditioned reflex, by extinction or differentiation or by some other means, as well as that conditioned reflexes of the same type to other stimuli are retained, sometimes even without perceptible changes in these reflexes. From these observations we may conclude that the cortical focus of the unconditioned reflex (US in Fig. 1) can also not be regarded as the site of the origin of conditioned inhibition.

We also have available findings obtained in our laboratories in the course of several years, which are in some ways more closely related to the question of the origin of conditioned inhibition in the elements of the conditioned reflex arc. For many years my colleagues and I have systematically investigated the problem of so-called switching* in conditioned reflex activity (Asratian, 1941, 1947). The essence of the matter is that it is possible to give a single indifferent stimulus two different signal meanings at the same time, for example alimentary and electrodefence, positive and negative, short delay and long delay, etc. This is done by reinforcing the stimulus differently in two different experimental situations (in different rooms, at different times of day, or by different experimenters, etc.), for example by reinforcement with food in one situation and with electric stimulation in another, by immediate reinforcement in one situation and delayed reinforcement in another, by reinforcement in one situation and non-reinforcement in another. Figure 2 illustrates schematically switching experiments conducted by my colleagues F. M. Shitov and V. V. Iakovleva (1937), and described in Chapter 4. Shitov, in morning experiments in dogs, paired a metronome beat of 120 strokes per min with food, and evoked an alimentary conditioned reflex;

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* See editor's footnote in Chapter 4.

Iakovleva, in afternoon experiments in the same room and on the same dogs, paired the same stimulus with electric stimulation of a paw of the animal and evoked an electrodefence motor conditioned reflex. The metronome thus served as two different signals for the animal: a food signal and an electrodefence signal. However, under actual experimental conditions, as a rule only one of the signals appeared, the other remaining in an inhibited state. In the morning experiments the metronome evoked only an alimentary conditioned reflex, and in the afternoon experiments it evoked only a conditioned electrodefence reflex.

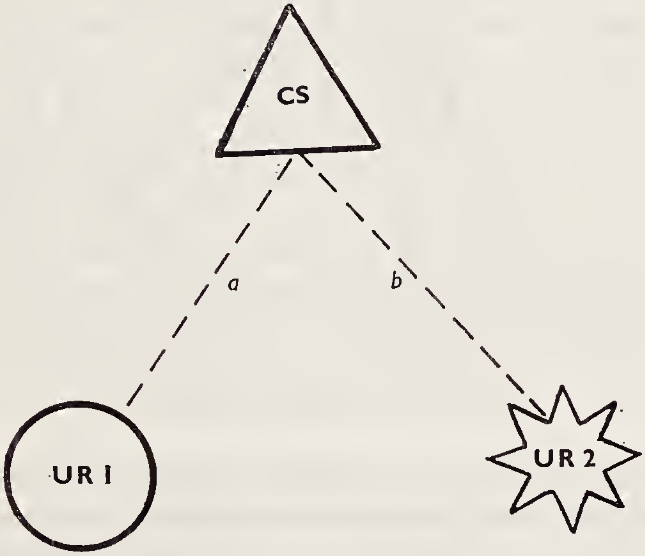

FIG. 2. Scheme of single switching. CS, conditioned stimulus; UR 1, unconditioned reflex No. 1; UR 2, unconditioned reflex No. 2.

These data are similar to those obtained recently in our laboratory by M. I. Struchkov (1955, 1956). He developed in dogs two conditioned reflexes of different types: an alimentary conditioned reflex to the sound of a buzzer, and an electrodefence conditioned reflex to tactile stimulation of the skin. When these reflexes had attained a considerable degree of definition and stability, Struchkov proceeded with parallel experiments on the same animals in another room, radically changing the character of the experiment: specifically, in the new room he paired the tactile stimulation of the skin with food, and the buzzer with electric stimulation of the paw. Eventually the dogs handled even this extremely difficult problem. After a phase of gradual increase in the intensity of adequate reactions and decrease in the intensity of inadequate reactions to each stimulus in this room, the animals reached a point where in one room the buzzer evoked only the alimentary conditioned reflex and the tactile stimulus only the electrodefence conditioned reflex, while in the other room the buzzer evoked only the electrodefence conditioned reflex and the tactile stimulus only the alimentary conditioned reflex (Fig. 3).

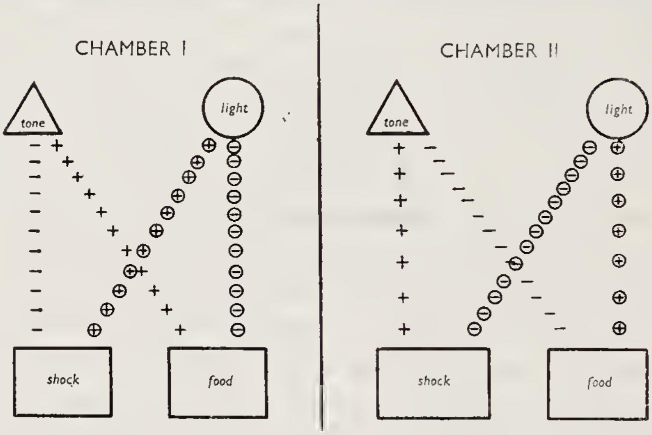

Fig. 3. Scheme of double switching.

It seems clear from these observations made by Shitov and Iakovleva, and by Struchkov, that the appearance of only one of the two conditioned reflexes evoked by this stimulus and the suppression of the other seems clearly to be the result of the development of a process of inhibition in those elements of the arc of the conditioned reflex that are, as it were, suppressed at the will of the experimenter. It is clear that this inhibition is not localized in the focus of the conditioned stimulus (since in each room the stimulus evokes one of the conditioned reflexes), nor in the foci of the unconditioned stimuli of different types (since, according to Struchkov's data, it is possible in each experiment to produce both alimentary and electrodefence conditioned reflexes). Therefore we must conclude that inhibition in these experiments originates and is localized in the nerve elements of the conditioned connection itself.

It is interesting to note that the two conditioned reflexes of different types evoked by one and the same stimulus are in an antagonistic reciprocal relationship. Inhibition of an active conditioned reflex, that is, one functioning in a particular situation, evoked by some stimulus (whether by extinction, by the influence of an extraneous stimulus, or by other means) involved the automatic disinhibition of the inactive "partner" conditioned reflex evoked by this same stimulus in the situation. This very interesting observation, which has repeatedly been verified, is further evidence of the correctness of the conclusions drawn concerning the development of inhibition in the structural elements of the conditioned connection itself.

Also of great interest from the standpoint of the question under discussion here, are the results of our experiments on switching of conditioned reflexes of the same type but with an opposite functional sign. I refer to the results of the unpublished experiments of F. M. Shitov and V. A. Zamiatina described in Chapter 4. The results of these experiments seem to support the view that chronic inhibition also is localized in the structures of the conditioned connection. If it were localized in the cortical focus of the conditioned stimulus, the conditioned reflexes inhibited in some experiments would not evoke a reflex in the other experiments. Also, if this inhibition were localized in the cortical focus of the unconditioned stimulus, in experiments of the second type the situation would not occur in which one stimulus evoked a conditioned reflex while another related stimulus did not.

We now have available some additional experimental material on the localization of conditioned inhibition, obtained in experiments of a different sort in which the same stimulus acquires simultaneously the signal values of two conditioned reflexes of different types, the alimentary and the electrodefence*. These differ from the switching experiments in that both meanings of the conditioned stimulus appear in parallel and simultaneously, under the same conditions and in the same situation. This is accomplished by pairing the same indifferent stimulus with food in some experiments and with electric stimulation of a paw in others, or by reinforcing the stimulus with food and shock simultaneously. The application of the conditioned stimulus then simultaneously evokes both the conditioned alimentary reflex and the conditioned electrodefence reflex. Figure 4 shows part of a kymographic recording of such experiments, conducted by my colleague

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* See editor's footnote in Chapter 4.

F. K. Daurova (1960). Moreover, it was found possible in the same animals to preserve the usual single conditioned reflexes to the other stimuli together with the new dual (or binary) conditioned reflexes.

Leaving aside all the material obtained in our laboratory regarding these dual conditioned reflexes, I will limit myself here to a brief description of only the findings which are directly related to the question of the origin and localization of conditioned inhibition in the elements of the conditioned reflex arc. Daurova experimented with the extinction of dual conditioned reflexes by repeated applications of the conditioned stimulus without reinforcing it with either food or electric shock. She found it possible to inhibit completely one of the dual conditioned reflexes, namely the alimentary, while preserving the other, i.e. the electrodefence conditioned reflex, for a long time (Fig. 5). It was shown by Daurova that when the stimulus is not reinforced both by electric current and by food, the extinction of both conditioned reflexes does not develop in parallel; one reflex is inhibited while the second is still present (Fig. 6).

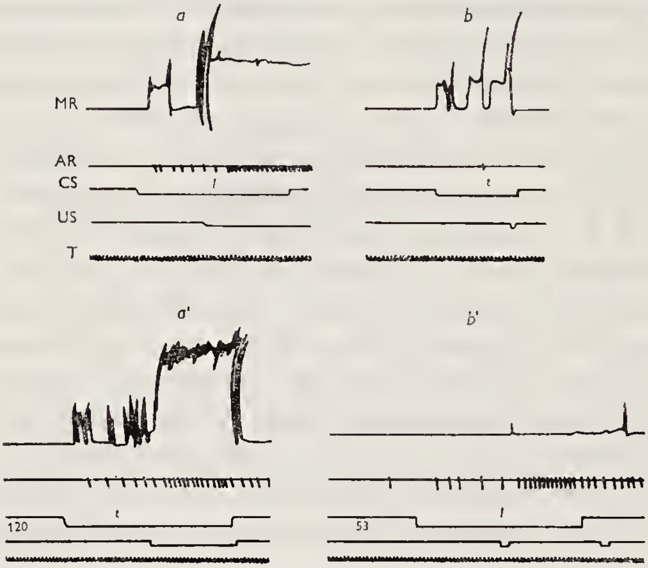

FIG. 4. Dual (a and a') and single (b and b') conditioned reflexes. MR, motor reflexes; AR, alimentary reflexes; CS, conditioned stimuli; US, unconditioned stimuli; T, time in sec; 1, light stimulus; t, tone stimulus. Figures indicate the number of pairings of tone (t) and light (1).

It will be noted that in these experiments, in contrast to experiments with switching, the conditioned stimulus evokes both reflexes at the same time in a single experiment and under the same conditions, and there is developed, not chronic inhibition of a single reflex as in the case of switching, but sudden inhibition which develops in the course of a single experiment. Therefore the data obtained in these experiments seem an especially illustrative and convincing demonstration of the theory that conditioned inhibition originates, not in the focus of the conditioned stimulus, but in the subsequent connecting elements of the conditioned reflex arc. Moreover, in view of the fact that after the extinction of one of the dual conditioned reflexes, the single conditioned reflexes of the same type to other

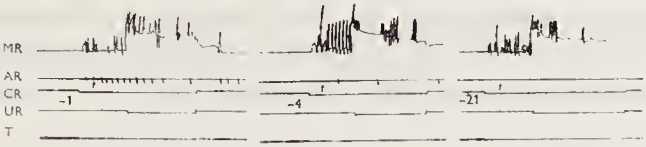

FIG. 5. Extinction of one of the dual conditioned reflexes. MR, motor reflexes; AR, alimentary reflexes; CR, conditioned response; UR, unconditioned response; T, time in sec; t, tone stimulus. Figures with minus sign indicate the number of nonreinforcements.

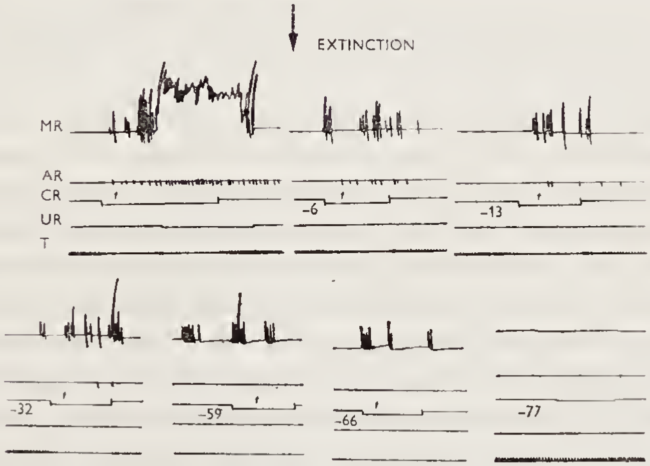

FIG. 6. Extinction of both dual conditioned reflexes. See the legend to Fig. 5 for the key to abbreviations. Figures with minus sign indicate the number of nonreinforcements.

stimuli persisted without significant changes, while after the extinction of a single conditioned reflex the same type of conditioned reflex in the dual reflex combination does not change, we may also conclude that this inhibition does not originate in the focus of the unconditioned stimulus (Fig. 7). There is again no alternative to the conclusion that conditioned inhibition originates and is localized in the elements of the conditioned connection itself.

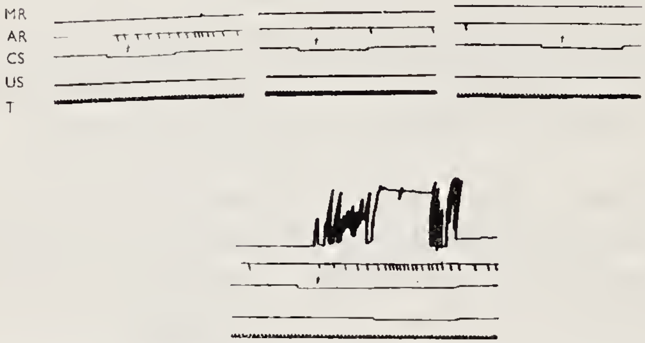

FIG. 7. Dual conditioned reflex after extinction of the single conditioned reflex. See the legend to Fig. 4. for the key to abbreviations.

Some experimental data on the question of the localization of conditioned inhibition have also been obtained in investigations which we recently carried out on the problem of bidirectional conditioned connections. I wish to supplement what I have said above by citing these data, and in order that they may be more readily understood I will first note that usually in our conditioned reflex experiments we pair two stimuli, each of which evokes an unconditioned reflex that can be objectively and accurately determined and graphically recorded. Examples of such stimuli are: food, electric stimulation of the paw, local cooling of a certain area of the skin (in order to evoke a local vasomotor reflex), puffs of air into the eye (to evoke the eyelid reflex), passive lifting of the paw (to evoke reflex relaxation of the extensor muscles, ascertained by the recording of the resultant electromyograms; subsequently, as conditioned reflexes are developed, the passive movements of the paw become active), etc. We pair these stimuli in different combinations, in either stereotyped or variable sequence. In this way bidirectional conditioned connections are usually developed: each of the paired stimuli eventually acquires the ability to evoke, together with its own unconditioned reflex, the reflex of the "partner" stimulus as a conditioned reflex. Figure 8 is a diagram of the arc of such a conditioned reflex. Omitting a detailed description of these reflexes and the experimental material which we have available, I will cite here only the data that pertain to the localization of conditioned inhibition in the reflex arc of these reflexes. Experiments of this type were carried out by our collaborators Varga and Pressman and by Struchkov, and are described in Chapter 5.

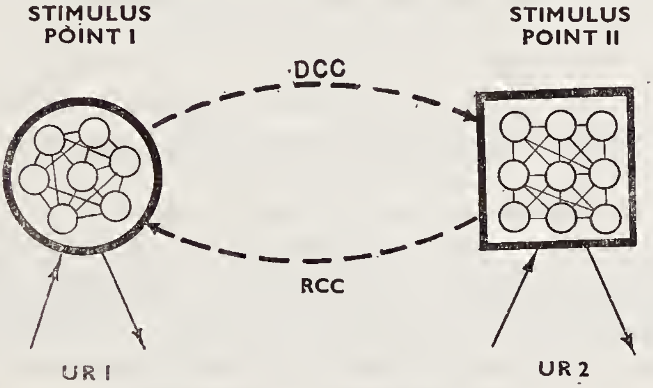

FIG. 8. Scheme of the conditioned reflex with bidirectional connection. DCC, direct conditioned connection; RCC, reverse conditioned connection; UR 1, unconditioned reflex No. 1; UR 2, unconditioned reflex No. 2.

Similar data were obtained by Struchkov (1960) with other bidirectional reflexes produced by pairing food either with passive lifting of a paw or with local cooling of a small area of skin on the animal's side. In the first variation, presentation of food evoked conditioned reflex lifting of the paw, and passive lifting of the paw evoked a conditioned alimentary reflex. In the second variation, presentation of food evoked a local skin vasomotor conditioned reflex, and cooling the skin evoked a conditioned alimentary reaction. When Struchkov carried out extinction of one of the bidirectional conditioned reflexes, i.e. when he presented food repeatedly without reinforcement by lifting the paw, presentation of food continued to evoke an alimentary reaction after the complete inhibition of the conditioned paw lifting which it had previously evoked, and also passive lifting of the paw during this period evoked a conditioned alimentary reflex (Fig. 9). Essentially the same results were also obtained with the extinction of the vasomotor reflex to the presentation of food.

The results of the experiments by Struchkov and by Varga and Pressman indicate even more clearly and convincingly than do the findings of our other colleagues which we described earlier, that conditioned inhibition originates and is initially localized precisely in the structures of the conditioned connection itself, and definitely not in the cortical foci of the conditioned and unconditioned stimuli.

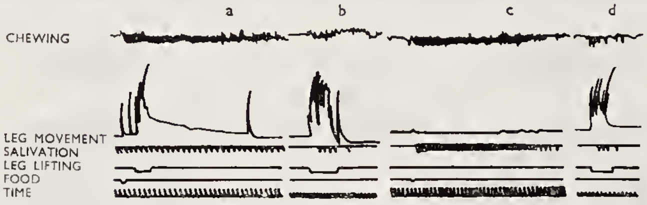

FIG. 9. The bidirectional motor defence and alimentary conditioned reflexes, shown in (a) and (b). The persistence of the alimentary reflex to the electric stimulation of the leg (d) is shown after extinction of the motor defence reflex to food (c). (a) the direct conditioned connection; (b) the reverse conditioned connection; (c) the extinguished direct connection; and (d) the test of reverse connection after the direct connection is extinguished.

On the other hand, as I stated above, I grant that when conditioned inhibition subsequently becomes more profound in the structures in which it originates, it can then spread both to the focus of the conditioned stimulus and to the focus of the unconditioned stimulus, i.e. it can to some degree include all the central components of the conditioned reflex arc. This is shown by a weakening of the unconditioned reflex, by a weakening of the original reaction to the conditioned stimulus, and by the development of a state of drowsiness and sleep. It is apparent, however, from the above statements that these phenomena, which have long been known through the great wealth of material from the Pavlovian laboratories, are interpreted somewhat differently by us than by the investigators mentioned above. Those who believe that conditioned inhibition originates in the focus of the conditioned stimulus or in that of the unconditioned stimulus, regard the phenomenon of the spread of inhibition as the result of a subsequent intensification of the initial inhibition in the foci of the conditioned or unconditioned stimuli. We suggest, on the other hand, that conditioned inhibition first arises in the structures of the conditioned connections, and that, as inhibition subsequently intensifies in these structures, it spreads to the foci of the conditioned and unconditioned stimuli and to other central nervous structures in general. The possibility has, of course, not been ruled out that in some conditions of an extraordinary sort inhibition can also originate in the foci of the conditioned or unconditioned stimuli and, subsequently becoming intensified in these structures, produce various results. Our data, however, give us adequate reason to believe that this does not usually occur and that, as a rule, conditioned inhibition originates in the structures of the conditioned connections, and only much later appears and becomes intensified in the foci of the conditioned or unconditioned stimuli.

In support of my theory, I wish further to cite the results of recent experiments by our colleagues L. I. Chilingarian and E. A. Romanovskaia (1960). These experiments were performed on dogs with previously implanted contact electrodes in the cortical motor foci of the paws, which made it possible under chronic experimental conditions to produce movements of the paw by means of electric stimulation of the corresponding cortical foci and to follow changes in the degree of excitability of these foci under the influence of various agents and factors. In these dogs, Chilingarian developed motor conditioned reflexes by pairing an indifferent tone with electric stimulation of the corresponding foci in the motor cortex. Romanovskaia, on the other hand, developed conditioned motor reflexes in these dogs by the conventional method of pairing an indifferent stimulus with electric stimulation of a paw. When the conditioned reflexes had been developed and had attained a certain degree of stability, the experimenters produced extinction of these conditioned reflexes, meanwhile following the dynamics of the changes (compared to their original level) in the excitability of the corresponding cortical foci by means of direct measurements. They both obtained similar data, as follows. In the course of the uneven extinction of the conditioned reflex, the excitability of the cortical motor foci was at first somewhat raised, then returned to its initial level, and later, as the conditioned inhibition intensified, there ensued a rapid fall in cortical excitability which finally led to a sharp and prolonged drop in the excitability of this focus below its original level. Sometimes the threshold value of the stimulating current increased to three, four or even more times its initial value. For comparison, I may point out that in the usual control experiments performed by these investigators in which extinction of conditioned reflexes was not produced, a shift of the opposite kind, i.e. a gradual and steady rise in the excitability of the cortical motor focus for the paw, usually occurred in the course of the experiment. This agrees completely with the data of many other investigators.

Although these experiments by Chilingarian and Romanovskaia are to some extent preliminary, and although the data obtained in them require further and more detailed investigation, nevertheless the reliability of the findings themselves is unquestionable, since they were checked in a large number of experiments on seven dogs of different types and ages.

Thus the data obtained in these experiments by direct recording, concerning the absence of significant changes in the excitability of the cortical focus of the unconditioned motor reflex in the stage of slight extinction and the significant decrease in its excitability in the stage of intense extinction, are in complete agreement with our other data described above. Specifically, they indicate that conditioned inhibition does not originate in the cortical focus of the unconditioned reflex but appears there later, after a marked intensification of inhibition.

We have at hand at present some experimental data concerning the origin and localization of another type of cortical inhibition, namely, supramaximal inhibition. Daurova obtained these data, which may be summarized as follows. In a series of experiments on switching, an alimentary conditioned reflex was developed in dogs to a tone with a frequency of 1100 c/s and an intensity of 45 dB in one experimental situation, and an electrodefence conditioned reflex was developed to the same stimulus in another situation. Both experiments were conducted on the same day, in no particular order. When both conditioned reflexes had attained a certain degree of stability and clarity of switching, Daurova performed experiments on supramaximal inhibition by increasing the intensity of the conditioned stimulus to 105–115 dB in both experimental situations. The results were very interesting: when the intensity of the conditioned stimulus was thus greatly increased, it ceased to evoke the alimentary conditioned reflex but continued to evoke the defense conditioned reflex, in other words it became supramaximally inhibitory for one activity while at the same time it retained its positive signal meaning for the other activity (Fig. 10).

Essentially similar results were obtained by Daurova in a second series of experiments on dual conditioned reflexes, in which she developed both alimentary and electrodefence conditioned reflexes to the same tone of 45 dB intensity, under the same conditions and in the same experiments. When both conditioned reflexes had reached a certain stability and the conditioned stimulus had evoked them both simultaneously quite strongly, experiments were performed to demonstrate supramaximal inhibition by means of a sharp intensification of the conditioned stimulus. These results proved to be the same as those in the previous series of experiments, i.e. the alimentary conditioned reflex disappeared but the electrodefence

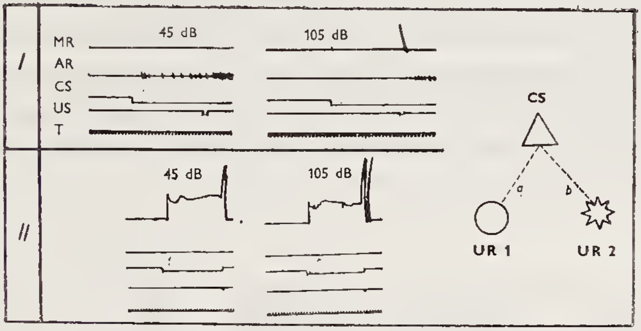

FIG. 10. Supramaximal inhibition on switching of conditioned reflexes. I, alimentary conditions; II, defence conditions; MR, motor reflexes; AR, alimentary reflexes; CS, conditioned stimuli; US, unconditioned stimuli; T, time in sec; TR1, unconditioned reflex No. 1; UR 2, unconditioned reflex No. 2; t, tone stimulus.

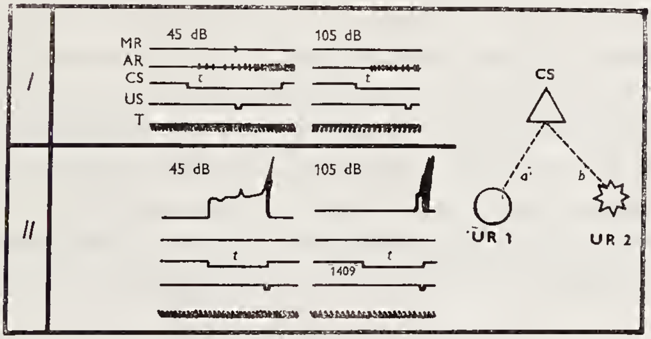

FIG. 11. Supramaximal inhibition on switching of conditioned alimentary (strong) and defence (weak) reflexes. See the legend to Fig. 10 for the key to abbreviations. In this experiment the food portion is doubled and the electric stimulation is weakened.

conditioned reflex remained (Fig. 11). On the other hand, in another series of experiments on switching and dual conditioned reflexes, Daurova increased the amount of food reinforcement for the 45 dB tone (70 g of meat-biscuit powder instead of 30 g as in the previous experiments), and greatly reduced the electric current (Fig. 12). When the conditioned reflexes had been developed, she performed experiments similar to those described above in order to demonstrate supramaximal inhibition by means of a sharp intensification of the tone. This time, however, the electrodefence conditioned reflexes proved to be inhibited and the alimentary reflexes were retained.

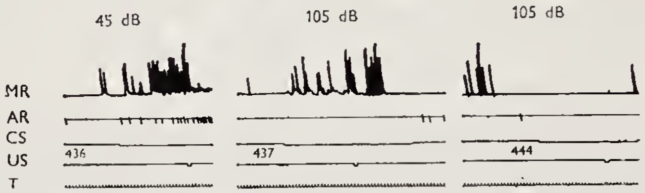

FIG. 12. Supramaximal inhibition with dual conditioned reflexes. See legend to Fig. 4 for the key to abbreviations.

The general conclusion from all these experiments is clear: since in response to the application of an extremely intense conditioned stimulus only one of the two conditioned reflexes normally evoked by that stimulus is inhibited, it is evident that the supramaximal inhibition is localized, not in the cortical focus of the conditioned stimulus as Pavlov believed and as is commonly supposed, but in the subsequent components of the conditioned reflex arc. The question of precisely which components are involved is at present being studied by Daurova.

In conclusion, I wish to make the following observation. In order not to complicate such a difficult task as this, I have deliberately not been concerned in this chapter with the problem of the mechanism of inhibition, with its nature, or with other aspects of the problem of inhibition. I wish to observe, however, that in our opinion the views of the investigator concerning the mechanism of development or the nature of inhibition are not of crucial importance to the question here under discussion.

In this chapter we have spoken constantly of the origin and localization of cortical inhibition. This is because we believe that, at least in the higher animals and in man, the conditioned reflex is coupled between two cortical foci and the conditioned connection passes through cortical structures. At present the question of the closure of the conditioned connection in the higher parts of the central nervous system, meaning the question of the localization of the central portion of the conditioned reflex arc, is the subject of intensive discussion. We have deliberately not been concerned with the existing theories on this problem for the same reasons for which we did not discuss the nature and mechanism of the origin of inhibition in the cerebral structures. Whatever theories an investigator holds on the question of the localization of the conditioned connection in cerebral structures is similarly of no essential significance to the question under discussion.

In conclusion, I wish to note my own great satisfaction with the fact that the results of the investigations which my colleagues and I carried out, have permitted us to develop somewhat further, and at a number of significant points to make more precise and to supplement the ideas of our great teacher Pavlov on the problem of inhibition, one of the most complex and important problems of higher nervous activity.

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